VOLUME 9 NUMBER 2

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FEBRUARY, 1924

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Archives of Dermatology and Syphilology

VOLUME 9 FEBRUARY, 1924 NUMBER 2

XANTHOMA TUBEROSUM

TWO NECROPSIES DISCLOSING LESIONS OF THE CENTRAL NERVOUS SYSTEM AND OTHER TISSUES *

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PHILADELPHIA

Although an uncommon condition, xanthoma tuberosum gives such a striking clinical picture and can be diagnosed so readily that unless there are additional features that reflect something of its cause, clinical reports alone are now passé. Necropsy reports are rare, but of these a sufficient proportion has disclosed analogous internal changes to indicate that in the future search for these should be made. In the first of our cases only the tendo patellae was affected in addition to the skin; but in our second case, the lungs, liver, skull, pineal body, pituitary and tuber cinereum were invaded, attaining, we believe, the high-water mark for extracutaneous xanthic involvement to date. Other features which threw sidelights on established or controversial phases of the disease were the association of xanthoma planum in Case 1, and of jaundice and hypercholesterolemia in Case 2.

REPORT OF CASES

CASE 1.—Russell G., aged 36, white, who had died of lobar pneumonia in the medical wards of the Philadelphia General Hospital, was seen by us for the first time on the necropsy table. The cutaneous lesions, except those of the eyelids had the classic distribution and individual characters of xanthoma tuberosum (not diabeticorum). There were hundreds of nodules distributed on the palms, the dorsa of the hands, the elbows, knees, buttocks and elsewhere; they were hard and yellow as usual, and the larger ones on the hands were ulcerated. The right upper eyelid bore a broad xanthoma planum lesion, and there was a small one on the lower lid near the inner canthus. These two were in no sense nodular —they were typical plane lesions. The other (left) upper eyelid bore three tuberous xanthoma lesions in a row, the largest being 3 mm. in diameter and the smallest 1 mm. The clinical course of the cutaneous disease appears to have been the usual chronic one. Blood chemical studies had not been made because the patient entered the medical service for the first time for his acute illness.

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* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, and the Laboratory of Pathology, University of Pennsylvania.

* Read before the Section on Dermatology and Syphilology at the Seventy-Fourth Annual Session of the American Medical Association, San Francisco, June, 1923.

Being an unclaimed subject, the whole body was secured and dissected at leisure, and an abundance of material was obtained for histologic study. None of the viscera were found to be affected by the xanthic process. Of the tendons, those of the dorsa of the hands (over the joints) and the tendo patellae contained more or less clustered nodules up to 1 cm. in diameter. Those in the latter were not continuous with the overlying skin lesions, but some of the nodules on the hand were.

Histologic Examination.—We have examined sections from a dozen different blocks of tissue, and have employed the histologic methods which Pollitzer and

Fig. 2 (Case 1).—Exanthoma planum of right eye. Larger lesion on upper lid and smaller one on lower. Museum preparation somewhat shriveled by preservative.

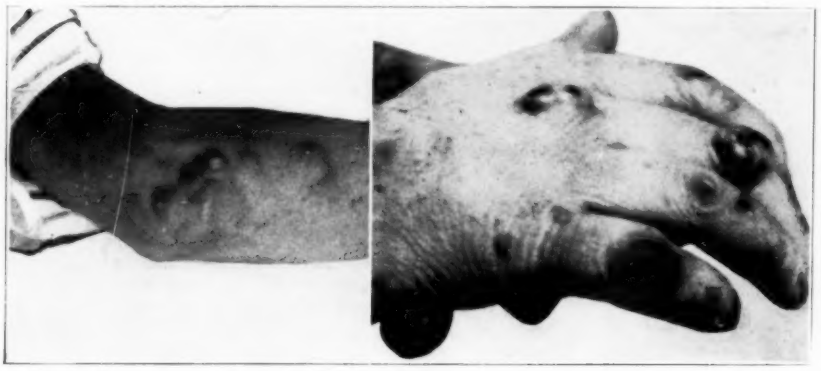

Fig. 3 (Case 1).—Tuberous lesions on hands and elbows.

Wile[1] used in 1912, and which Lebedew[2] repeated in 1913. We join the army of workers that has confirmed their splendid morphologic findings, including the polariscopic ones. However, since the status of xanthoma histology may now be considered as established, and its pathogenesis all but stabilized, as expressed

1. Pollitzer, S., and Wile, W. J.: J. Cutan. Dis. **30**:235-241, 1912.

2. Lebedew, A. J.: Dermatologia, St. Petersburg **1**:117-242-361 (Jan.-June) 1913.

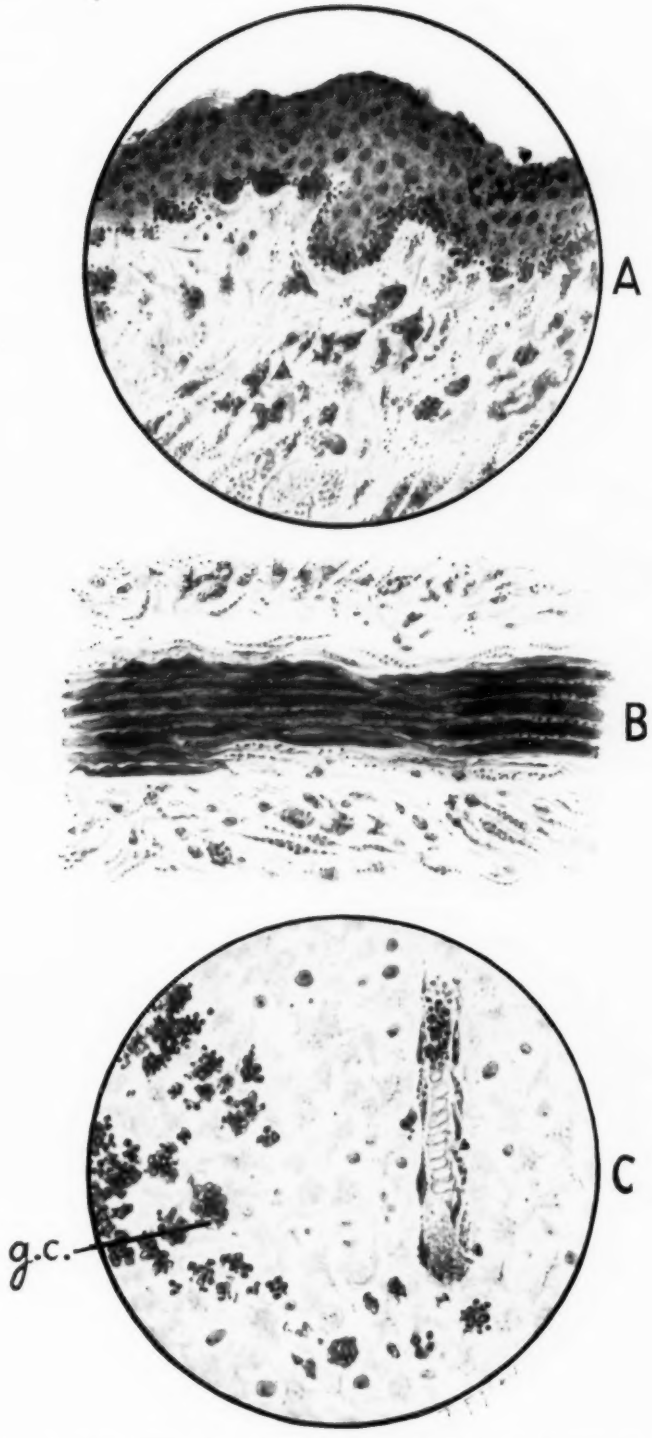

Fig. 1.—*A*, skin from Case 1 showing xanthic change in rete cells immediately above a tuberous lesion. Fat may be seen in the xanthoma cells of the corium also; that is, both epithelium and connective tissue are affected. *B*, arrectores pilorum muscle coursing through a tuberous xanthoma of buttock (Case 1)—xanthic change in muscular tissue. *C*, capillary and glia cells (*g. c.*) in tuber cinereum (Case 2). This field was at the extreme margin of the xanthoma. This illustrates the xanthic change in nervous tissue. Sudan III and hematoxylon preparations.

by Darier[3] in his textbook of dermatology, we will not describe our sections in detail, but dwell only on features which appear to be additions to the general fund of knowledge or which need to be emphasized.

Early lesions on the buttock from 1 to 3 mm. in diameter were selected and some sections were imbedded in paraffin and some were frozen. The already established histology of xanthoma tuberosum was revealed. Thus, the increased bulk which was responsible for the nodule clinically was due chiefly to hyperplasia of white fibrous connective tissue cells, followed by a transformation into "xanthoma cells." We agree with Pollitzer that the latter in part at least is a "collagen" cell which is undergoing the fatty change, for we have seen the fat droplets within such cells as Low[4] figures them while they were still as

Fig. 4 (Case 1).—Xanthoma planum of the right eyelid. The swelling on the upper surface is the xanthic part. Note the independence of the orbicularis palpebrarum fibers below from the xanthic lesion above. Irregularly staining tarsal plate below.

integral a part of the collagen bundle as they are in normal collagen, and at a time when they were not within lymphatic spaces. These cells could not by any stretch of the imagination be interpreted as being endothelial. Both Sudan III and copper hematoxylin[5] stains brought this out admirably. We have also seen

3. Darier, J.: Textbook of Dermatology, English trans. by Pollitzer, New York, Lea & Febiger, 1920.

4. Low, R. C.: Brit. J. Dermat., April, 1920.

5. Klotz, Oscar: J. Exper. Med. **7**:663, 1905; **8**:322, 1906.

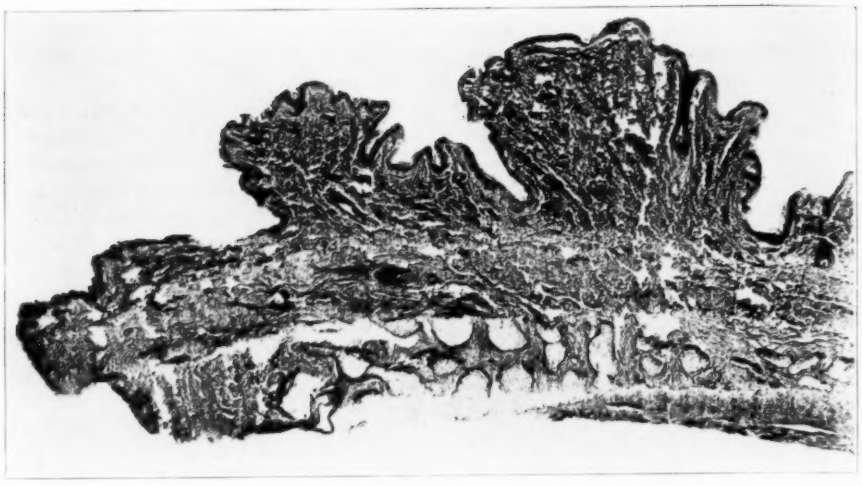

Fig. 5 (Case 1).—Xanthoma tuberosum of left eyelid.

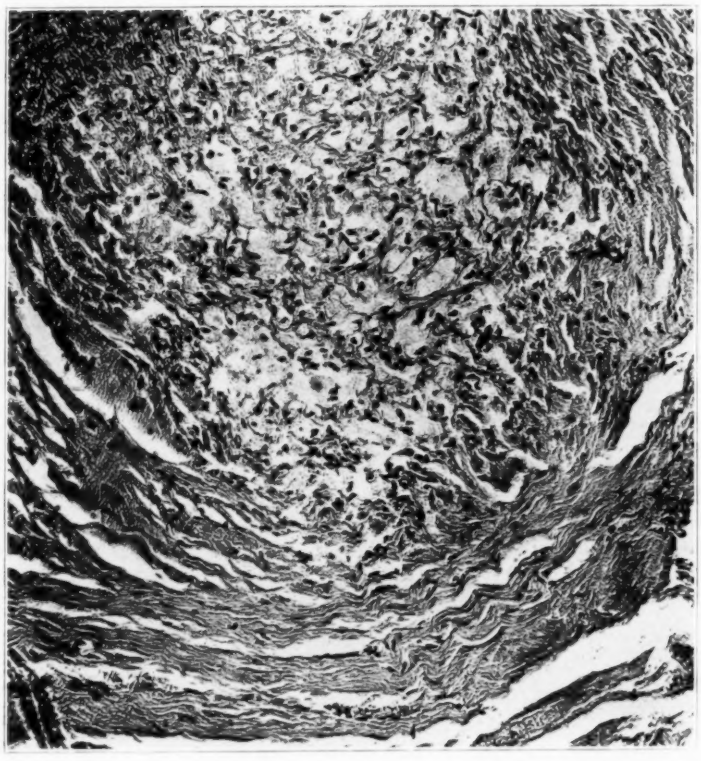

Fig. 6 (Case 1).—Xanthic nodule of tendo patellae.

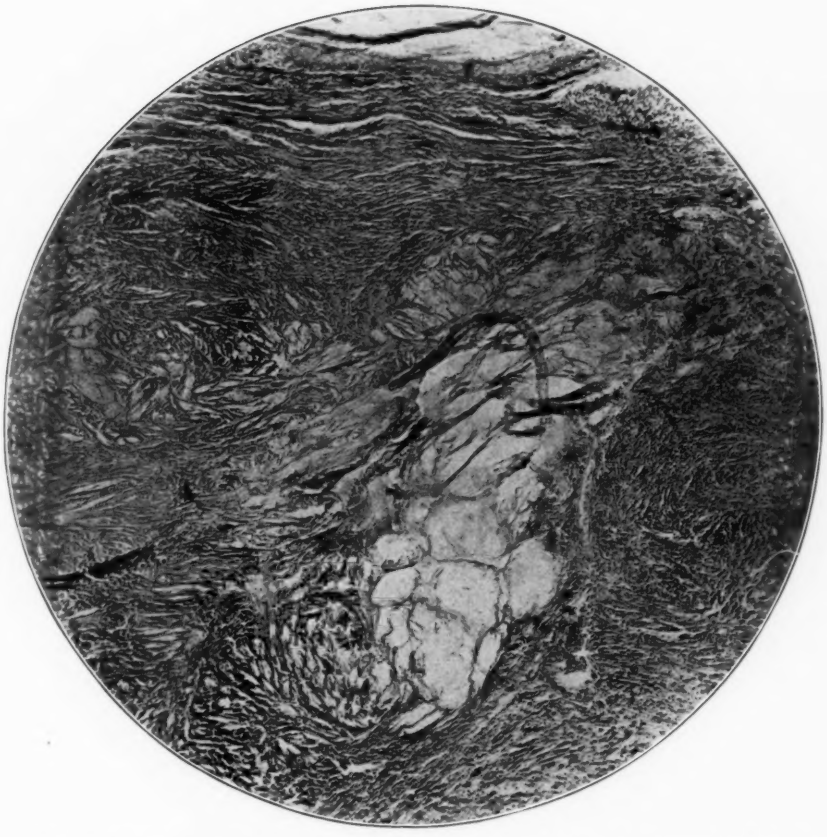

Fig. 7 (Case 1).—Tuberous lesion from skin of buttock, demonstrating the larger and smaller cholesterol clefts.

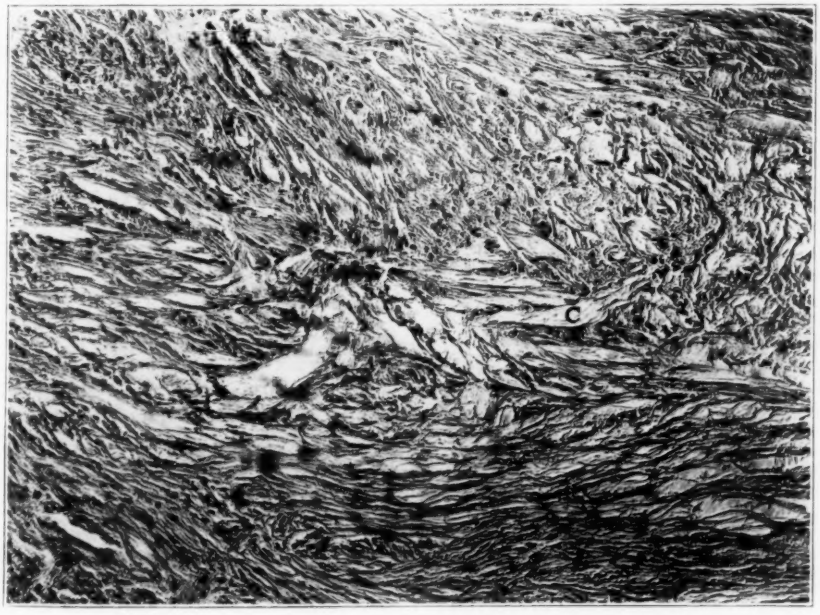

Fig. 8 (Case 1).—Lower left hand corner of Figure 7 more highly magnified. Shows the cholesterol spaces within the collagen bundles (at *C*, for instance).

the minute whetstone and needle-like crystals within these cells, some of which were stained by Sudan III and by copper hematoxylin. These fatty substances were also extracellular in places and clogged the lymphatics.

The histologic features which we believe we report for the first time are three: First, whereas cholesterol crystals (plates) have already been mentioned as occurring within lymphatic[6] spaces, we believe that we have demonstrated them for the first time *within* the collagen bundle. This is important clinically because it partly answers the objection which Essickson has raised that the strikingly yellow color seen clinically could not be explained on the basis of the xanthoma cells alone. There is thus a lipoidal degeneration of the collagenous fibrils themselves which adds its quota to the sum total of yellowness; and it is possible that the yellow color is even further affected by a lipoidal degeneration of the collagen itself which is of a grade and kind not sufficient to be manifested histologically, but which is still sufficient to change the normal protein grayness to yellow. This possibility has become an established fact in kidney degeneration—the fat phanerosis of the general pathologist. In passing, we note that Siemens[7] has recently expressed an opinion that this yellowness may be due to carotin and xanthophyll.

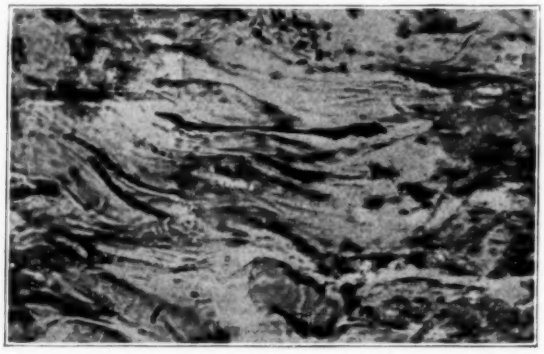

Fig. 9 (Case 1).—Sudan III preparation of plane lesion from right eyelid. Outlines of collagen *cells* (not the nuclei thereof) brought out in a unique manner, appearing black by reason of the fat they contain.

We demonstrated this intrafascicular cholesterol morphologically by teasing the collagen bundles with needles from frozen sections under the microscope, and observing that certain still intact bundles were almost solidly composed of the characteristic plates with notched corners. We are led to make this test by the appearance of the paraffin sections, in which the characteristic clefts once occupied by this lipoid appeared to be within, and not between, the collagen bundles; but this appearance needed the confirmation which the dissection tests furnished.

The second observation is important in respect to the eternal question whether xanthoma tuberosum and xanthoma planum are identical diseases, with, in our case, an identical histology for the tuberous and plane lesions which occurred on the two upper eyelids. The histologic appearance was the same as in older

6. Johnson, quoted by Pollitzer and Wile, footnote 1.
7. Siemens, H. W.: Arch. Dermat. u. Syph. Orig. **136**:159, 1921.

tuberous lesions elsewhere, except that there was none of the important fibrous hyperplasia peripherally. There was the usual accumulation of xanthoma cells around blood vessels and an unusually clear-cut transformation of collagen bundles into xanthoma cells. The orbicularis palpebrarum muscle was particularly studied. It lay well below the xanthic lesion, and it did not extend into the lesions.

In view of the clinical circumstance that the lesion on one upper lid was nodular whereas on the other it was plane, and in addition that the histologic findings showed an identity not only between the two but with tuberous lesions elsewhere, we believe that in our case at least xanthoma planum and xanthoma tuberosum lesions were one and the same disease manifestation.

The third observation was the advanced xanthomatous change noted in the arrectores pilorum in several sections. The fibers became swollen and so crowded with fat globules that the nucleus was scarcely distinguishable.

CASE 2.—*Clinical Course.*—Griffith[8] has already published the clinical data on our second case, and the patient has been shown[9] at a meeting of the Philadelphia Dermatological Society. In these two reports careful and detailed clinical considerations have been recorded, in the former with illustrations. Necropsy phases will therefore be emphasized.

This 9 year old boy was emaciated, jaundiced, polyuric and had an enlarged liver. His present condition dated back six years, beginning with temporary liver enlargement. One year prior to administration he had injured his head, and the infected site had been curetted. On presumptive grounds, he had received some incomplete injections of mercury, and immediately after this jaundice began. The cutaneous eruption began eleven months ago; that is, at about the same time. The nodules were grouped below the mouth, at the back of the neck, in the axillae, on the elbows and knees and in the lines of the palms. The margins of all four lids bore long plane lesions. There were several nodules on the side of the head; the underlying bone was depressed, and roentgenograms showed small bony defects of the frontal and parietal regions. Yellow as usual, the nodules were of the diabetic type, having definitely inflammatory peripheries; and, particularly in the axilla, they showed a central hair, that is, the lesion was perifollicular. There was a generalized hypertrichosis, the hairs being pale and silky. Among other laboratory findings the blood sugar was reported as 0.06 per cent., blood cholesterol 397 mg. per 100 c.c., and the Wassermann reaction negative. We regret that examination was not made for pentose.

Pituitary extract, hypodermically, reduced the polyuria and polydipsia markedly, but there was no corresponding effect on the cutaneous lesions. The patient left the hospital unimproved, and died thirteen months later. In this interval he developed a new tumor over the frontal eminence, and it was noted that the hair came out easily.

Postmortem Findings.—Besides the cutaneous lesions, conspicuous changes occurred in the liver, lungs, lymph nodes, calvarium and brain. The histologic descriptions which follow are based on sections stained with hematoxylin and eosin. All tissues showing xanthic change were stained by Sudan III and

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8. Griffith, J. P. C.: A Case of Xanthoma Tuberosum, with Early Jaundice and with Diabetes Insipidus, Arch. Pediat. New York, Treat & Co., May, 1921.

9. Freeman, W.: Xanthoma Tuberosum Multiplex Complicated by Enlarged Liver, Jaundice, Diabetes Insipidus, and other Conditions, Arch. Dermat. & Syph. **5**:286 (Feb.) 1922.

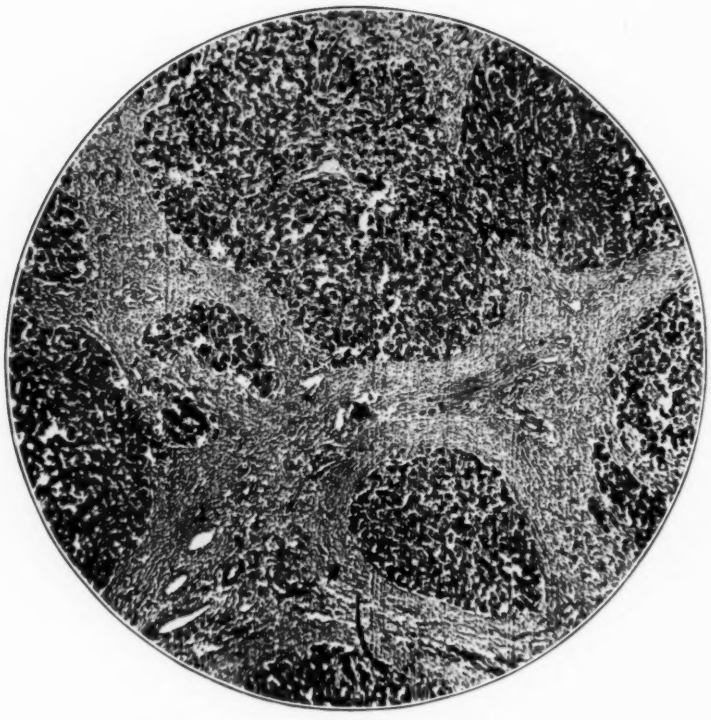

Fig. 10 (Case 2).—Cirrhotic liver.

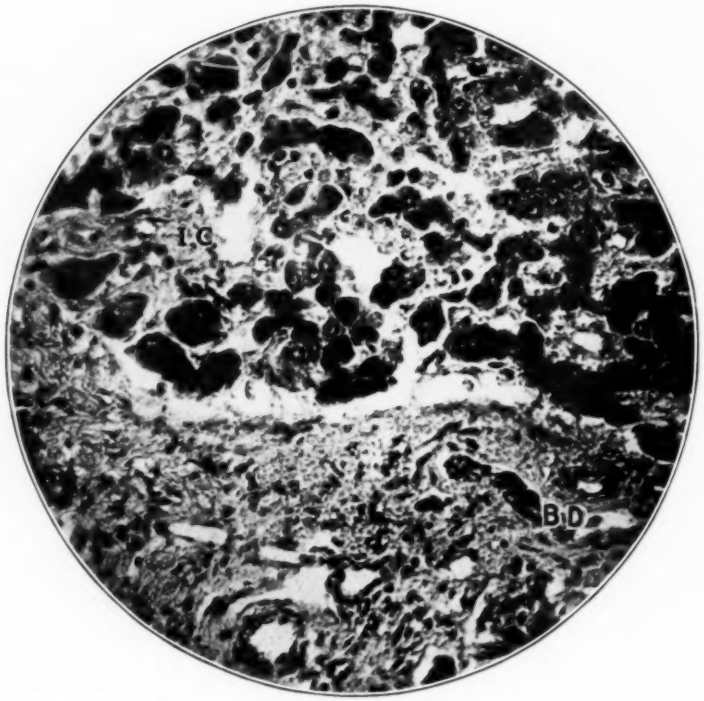

Fig. 11 (Case 2).—Cirrhotic liver; hyperplastic perilobular fibrous tissue below. Characters of the hypertrophic biliary form of cirrhosis are brought out in the form of intralobular penetration of fibrous tissue (*I.C.*). The liver cells appear so dark largely because they contain so much bile pigment. One of the hyperplastic bile ducts is located at *B. D.*

scharlach R, the skin with osmic acid in addition, and the nervous tissue by phosphotungstic acid hematoxylon, van Gieson's stain, cresylechtviolet and by Weigert's method.

The liver was enlarged, slaty green, and had a nodular surface, hypertrophic biliary cirrhosis. At the hilum there was a mass which enclosed the right and left hepatic ducts. On applying Sudan III to slabs of liver fixed in solution of formaldehyd U. S. P., pink points could be seen with the naked eye, thickly interspaced through the thickened interstitial tissue.

Microscopically, the picture of hypertrophic biliary cirrhosis was presented. In addition to the usual interlobar fibrosis with its hyperplastic bile ducts and lymphocytic and pigmentary infiltrate, there was a more or less delicate exten-

Fig. 12 (Case 2).—Xanthic portion of scar at hilus of liver.

sion of fibrous strands between the strands of liver cells in the lobule. The liver cells themselves were loaded with bile pigment and showed the accepted degenerative changes of this cirrhosis. There were no xanthic changes recognizable in these parenchymatous cells, but on staining frozen sections with Sudan III some of the interlobular fibrous tissue elements were found to be thus affected. More pertinent changes were found in the mass from the hilum. This was found to consist of fibrous tissue of a nonspecific inflammatory type, with no focal or other lesions to point definitely to syphilis. In it there were irregular heavy and diffuse lymphocytic infiltrates, but none of the circumscribed ones such as were seen in the lung. Blood vessels were numerous, the larger ones having heavily fibrosed walls and one or two showing calcification in addition. In certain areas extensive xanthic changes were present, but they were

never circumscribed and did not occur especially in relation to blood vessels, as is usual in the cutaneous expressions of the disease. At one end of the section the atrophic mucous membrane of the bile duct was shown, and below it appeared islands of its mucosa which had been snared off as the fibrosis developed. The interpretation placed on the appearance here was that most of the mass consisted of inflammatory fibrous tissue which may or may not have been syphilitic, and that parts of it had become secondarily xanthic. It is regretted that the histologic appearance in none of the internal organs was sufficiently characteristic to indicate positively some specific affection.

The lungs were tough, showed emphysematous bullae at the margins and stellate, yellow fleckings and plaques up to 2 cm. in diameter on the pleura, and

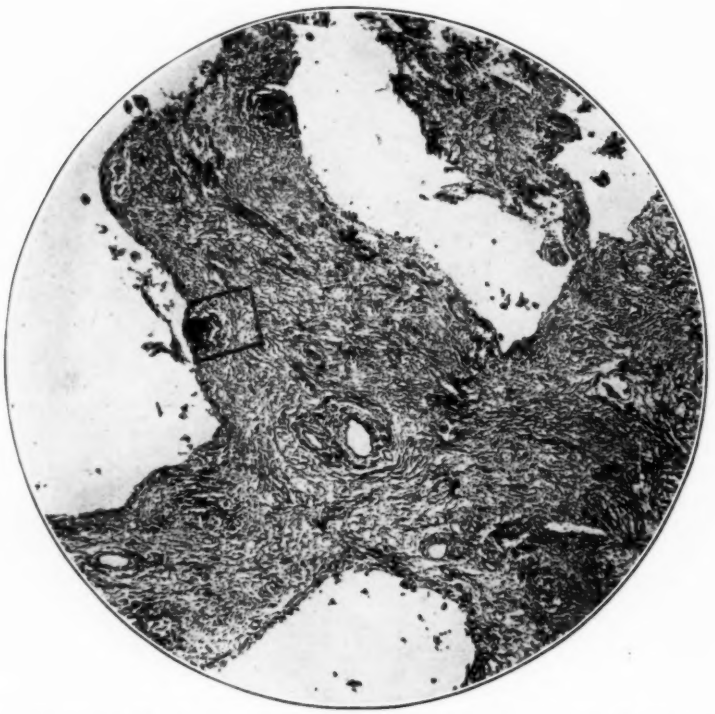

Fig. 13 (Case 2).—Fibrosed and emphysematous lung with diffuse xanthic change and lymphoid foci.

on incising appeared much like a rubber bath sponge; that is, there was marked fibrosis, together with emphysema. On the cut surface, diffuse yellow mottlings could be made out, but no definite tumors.

Microscopically, the basic features were those of brown induration. The alveolar walls were thickened almost beyond recognition, appearing as broad trabeculae of fibrous tissue rich in blood vessels. The alveoli were huge, and contained more or less desquamated alveolar epithelium, bile pigment and "herz-fehlerzellen." The latter were also to be found in the alveolar walls. The special additions to this basic picture were: (1) diffuse patches of xanthic change like those seen in the liver, and (2) nodal accumulations of lymphocytes, both

of these lying in the interstitial tissue. The latter could not be inflammatory in nature because they were so sharply aggregated, circumscribed and densely packed. We regard them as hyperplastic lymphatic anlagen.

The peribronchial and prevertebral lymph nodes were moderately enlarged, softer than normal and brownish red. Under the microscope they showed the features of hemolymph nodes. The medullary sinuses were hugely distended, and while they contained some plasma cells (mostly eosinophilic, and with coarse spherical granules), swarms of lymphocytes loaded with hemosiderin were the outstanding contents. A few of the latter had nuclei conforming to those of plasma cells, but the overwhelming majority had small solid nuclei. The outlines of these pigmented cells were indefinite and irregular—in fact, it appeared as though the degenerate cytoplasm and its contained granules was disintegrating

Fig. 14 (Case 2).—Lung showing focus of lymphocytes at left and xanthic change elsewhere. From portion of Figure 13 enclosed by rectangle.

and becoming intermixed with the medullary lymph. There were few polymorphonuclears and desquamated endothelial cells. All of the cell types described in the sinuses could also be found, but in smaller numbers, in the lymphatics of the capsule and general fibrous stroma of the nodes.

Nothing relative to the xanthomatous process can be postulated from what appeared in the lymph nodes, certainly not in connection with the hemolymph features. There was no fibrosis, no acute inflammatory reaction, or xanthosis. For our purposes, these nodes can be useful only in a small and suggestive way. Thus, since their cortical follicles so closely resembled the lymphoid nodes in the lung, they assist in identifying them. Secondly, since hemolymph nodes are developmental defects, they rather harmonize with our idea of the xanthic

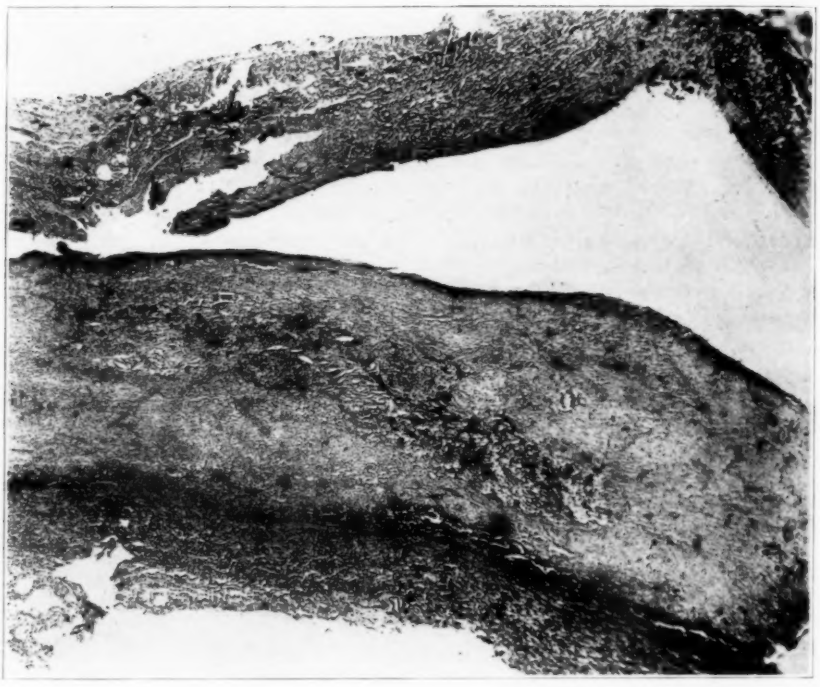

Fig. 15 (Case 2).—Skull "tumor." Low power magnification showing partially detached periosteum above. There is none of the original osseous tissue in the fibrous plate below. The clefts in it contained cholesterol.

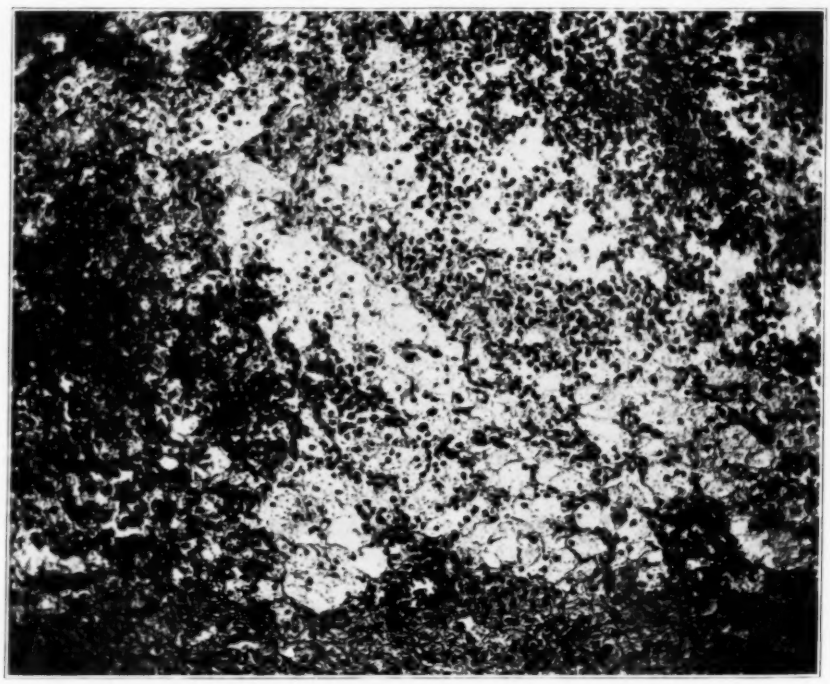

Fig. 16 (Case 2).—Details of Figure 15; heavy inflammatory round cell infiltrate and many "xanthoma cells."

process which was associated with them—at least if the lipoidal metabolism in this boy was not actually a congenital defect, it is reasonable to suspect that it was potentially so, just as in that other fatty dyscrasia, obesity.

On reflecting the scalp, two large fibrous depressions were found over the frontal and parietal regions, measuring 2.5 by 2 cm., and perhaps a score of smaller, bright yellow ones up to 6 mm. in diameter scattered over all parts of the calvarium. The two larger ones were fibrous, with no bony intermixture. In the parietal lesion, there was a flat, bright yellow mass occupying the entire interval between the pericranium and the dura, to both of which it was adherent. To one side of the center of the depression a hole 8 mm. in diameter extended deeply enough to disclose the brain surface. The smaller lesions elsewhere were sur-

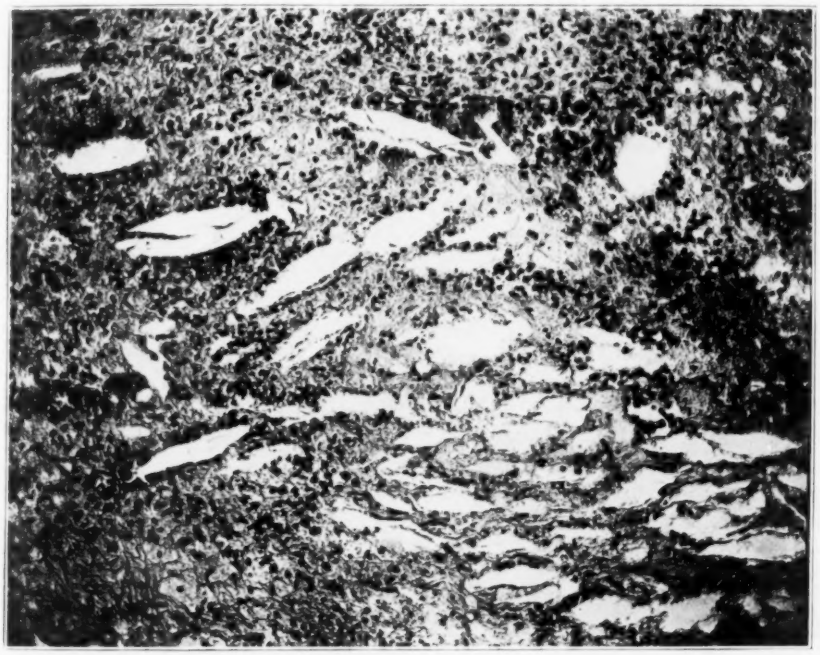

Fig. 17 (Case 2).—Tumor in skull showing cholesterol clefts and diffuse lymphocytic infiltrate.

rounded by a darker, slaty ring of discoloration. The calvarium was thin and brittle—almost eburnate.

In sections the dura and pericranium could be recognized as thick but vital fibrous strata which were in part continuous (adhesions) with an intervening chronic inflammatory tissue which had evidently been substituted for the bone. Only a few calcareous spicules remained to mark the presence of the latter, one or two of them showing barely sufficient osseous histology to distinguish them from calcareous infiltration. The inflammatory tissue was of old fibrous type. In places it was vital, in which case notable lymphocytic infiltrates and blood vessel hyperplasia were often associated similiar to those described in the liver mass. In other places it was necrotic or nearly necrotic, and in such

places there was an extensive xanthic change, together with numerous large clefts containing cholesterol (and probably other lipoidal bodies). The notched crystals of cholesterol were readily demonstrable in such clefts in frozen sections and by teasing bits of the lesion with needles. Few giant cells were present, and these were small, well enough developed, and lay adjacent to cholesterol clefts. The changes on the whole were like those seen so frequently in atheromatous plaques of the aorta—a marked inflammatory fibrosis, succeeded by such regressive changes as hyalinization, fatty degeneration and necrosis.

The dura was adherent to the pia only (and but slightly) at the margins of the hole above described. It was adherent to the calvarium, particularly in the parietal region, and less so beneath the small lesions.

In the brain tissue itself there were no yellow foci, except around the pineal and the pituitary bodies. The pituitary body was small, dark and friable. The posterior part and the stalk were large, hard and bright yellow. On median sagittal section through the interpeduncular space (brain fixed in solution of formaldehyd U. S. P.) a yellow, ovoid, apparently laminated tumor 10 by 7 mm. was found between the optic chiasm and the mammillary bodies. It was easily shelled out and was continuous with the stalk of the pituitary; that is, the xanthic process was a regional one extending both into the pituitary and the cerebral substances.

In dissecting out the gasserian ganglion, the epidural tissue around the basilar portion of the sphenoid was found to be xanthic. Circumscribed collections of this yellow tissue up to 5 mm. in diameter sprang apparently from the tissue around the left carotid artery close to the ganglion and cavernous sinus. There were other smaller yellow granules in the vicinity. The floor of the sella turcica was thin and easily perforated. The sphenoid sinus appeared to be normal.

The pineal body was enlarged (7 mm. in diameter) hard, round and uniformly yellow on the surface. On section it was found to be mottled yellow and did not grate.

In sections, typical xanthic changes were found in the parts of the nervous system that have been mentioned, consisting of numerous xanthoma cells interspersed in more or less fibrous tissue. The lymphocytic infiltrates, however, such as were seen in the liver and the skull, were decidedly in the background, and necrosis was not seen. We wish to emphasize that in the pineal body and tuber cinereum the xanthic process, including the underlying fibrous hyperplasia, was in a much more advanced state at the periphery, that is, toward the meninges; and in numerous instances the usual habits of xanthic extensions (along vessels) could be made out proceeding from the pia. It is thus felt that the causal pathologic influences have been centripetal, extended from the meninges inward.

We must record certain additional or special histologic details in several parts. Thus, in the pituitary body the posterior lobe was completely and diffusely fibrosed and xanthic, and although the anterior lobe was not sharply separated from the posterior, its glandular cells were relatively normal, and only a few xanthoma cells appeared between them. The pineal body was sheathed by a thick stratum of dense xanthic change which included some small cholesterol clefts. It was here that the extension of the xanthic process from the periphery to the center was most definite. Psammoma bodies were scarce.

The effect of these lesions on the histology of the brain tissue was, on the whole, not conspicuous. Excepting the tuber cinereum lesion, the tissue affected was glial, and even in the former the damage to cortical nerve cells was not

marked or extensive (the lesion was less than 1 cm. in diameter). The condition of the parenchyma of the tuber cinereum resembled tuberculoma—the boundaries were fairly distinct, and there was a local reaction on the part of the neuroglia. But there was no capsule, and nearby ganglion cells showed slight evidence of compression. Sections taken from various parts of the cerebrum showed only minor alterations in the ganglion cells.

From the standpoint of the general pathologist, we have been much concerned as to whether the hyperplastic changes which resulted in the "tumors" occurred in the glia cells or the fibrous tissue. Can nervous connective tissue undergo xanthic change as does white fibrous tissue? Sections stained with

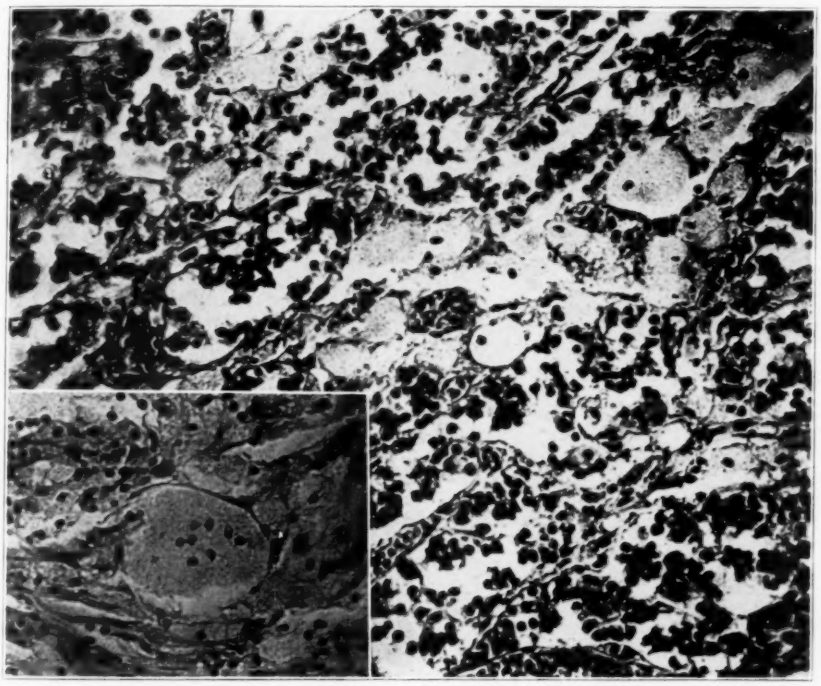

Fig. 18 (Case 2).—Xanthic change in pituitary body. "Giant" xanthoma cell in insert from another field.

van Gieson's stain, Mallory's analine blue connective tissue stain, and phosphotungstic acid-hematoxylin gave confusing or contradictory results; but taken in conjunction with purely morphologic considerations, they led us to the conclusion that the greater part of the xanthic change occurred in the hyperplastic white fibrous connective tissue cells. The deep green color of the tumor after fixation in solution of formaldehyd U. S. P. also pointed to this, since nerve tissue is one of the few tissues that are spared by the bile staining processes in jaundice. By careful search patches of degenerate cells in the tuber cinereum were finally identified as glia cells by reason of the still attached dendritic processes. These cells were markedly degenerate; their cytoplasms were cloddy,

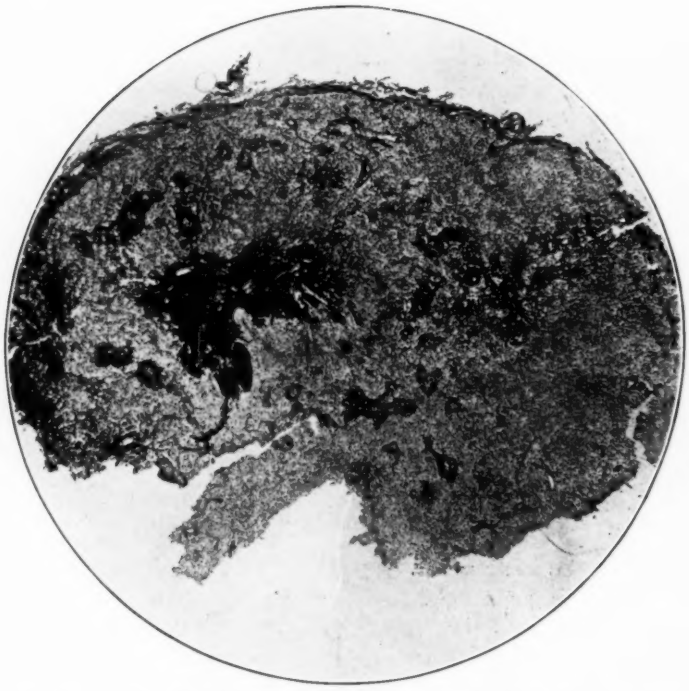

Fig. 19 (Case 2).—Sudan III preparation of pineal body. Xanthic parts are black.

Fig. 20 (Case 2).—Xanthic change in pineal body.

their outlines irregular and obscure, and certain ones had sufficiently foamy cytoplasms and sufficiently pyknotic nuclei to admit them to the category of the xanthoma cells.

In connection with the foregoing we must introduce the question of the scope and limitations of the xanthoma cell as it occurs in nervous tissue (not from the morphologic standpoint but from that of intracellular pathologic processes) because glia cells become rarefied and take on quasixanthoma qualities in a variety of retrogressive conditions which go under the general caption of softening. There are so many pros and cons concerned that they cannot be put down here; but the deciding factor which leads us to catalogue the glia cells of our case as xanthic is that fat is seen within the cells of an

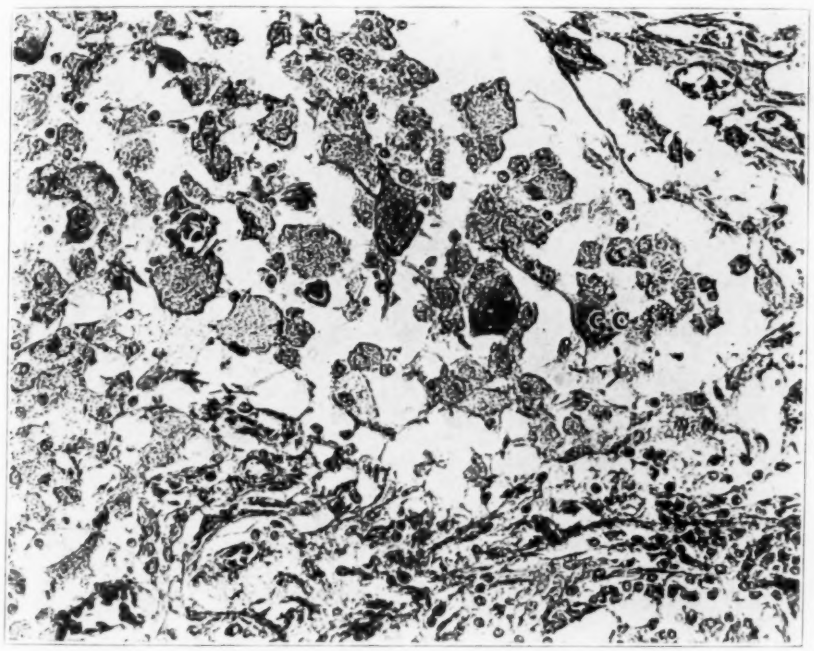

Fig. 21 (Case 2).—Tuber cinereum lesion. Xanthic change in glia cells. Mallory's connective tissue stain. Dendrites still attached to glia cell at *G. C.* Other cells are more severely xanthic.

obvious xanthoma of the brain, that some of these cells can be identified as glial and that transitions can be traced between the two. A full consideration of the subject of gliosis is given by Spielmeyer.[10]

Other organs at most reflected only the general sclerosing systemic affection which made so many of the tissues of this 9 year old boy resemble, particularly under the microscope, those of a subject dying of senility. We recount them briefly.

10. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922, p. 312-314.

There were one or two minute fibrous nodules on the margins of the mitral and tricuspid leaflets. Their yellowness must have been due to the jaundice alone, for no xanthic change appeared in the sections. There was a little fibrosis of the tips of the papillary muscles which extended somewhat into the myocardium, but there was no xanthic change in it (proved histologically).

The spleen was very large (14 by 9 by 4 cm.); otherwise it was normal grossly. Microscopically, there was a slight fibrosis of the trabeculae and a notable one of the reticulum. In the former, there were some foci of calcification (compare arteries of the liver). The splenocytes were reduced in number.

The kidneys showed only a passive congestion. Both ureters were uniformly dilated, averaging about 1 cm. in width through their whole course. The bladder appeared normal, and no obstruction was found to account for the dilated ureters.

The suprarenals were small, thin and flat, but otherwise appeared normal. In sections the zona fasciculata was found to contain abundant lipoid material in its peripheral parts, but mesially the cell cytoplasm lacked the globules. Considered on the whole, there must have been a marked reduction in the lipoid content of the suprarenal, but no more than is seen in many other conditions. The pars reticularis showed early autolytic change, and the medulla was normal.

The stomach, esophagus and intestine appeared normal, both grossly and microscopically.

The spinal cord appeared normal, both grossly and microscopically.

During life, nodules were excised from the knee and subjected to the special fat stains, among others scharlach R, Sudan III, osmic acid, Nile blue sulphate and copper hematoxylin. Except to demonstrate that the lesion was disposed immediately around a hair follicle, nothing more than is usually seen and reported in xanthoma tuberosum lesions was brought out. There was no lymphoid hyperplasia, simply the fibrous hyperplasia and xanthic change. At necropsy one of the axillary lesions was excised, and the sections presented a most striking appearance. Superimposed on the usual picture of xanthoma tuberosum was a hyperplasia and an enormous engorgement of the blood vessels— sufficient to simulate a hemangioma and make one question for the moment whether this was not a nevus which had become secondarily xanthic. MacDonagh[11] has described such cases and comments on one that showed angiomas interspersed among the xanthic elements. In our case, however, we feel that the vessels were too regularly disposed, too regular in caliber and too continuous to be neoplastic. Their engorgement was probably due chiefly to postmortem stasis, which had thus performed the service of an injection process and emphasized both the abundance of the blood supply in this lesion and the concentration of xanthoma cells around the blood vessels. A similar concentration around the hair follicles could not be made out here as it was in the biopsy material, because the process was so far advanced that it had affected every part of the corium. The hair follicles were overdistended with keratinous detritus, and no normal hair shafts were found within them. The hairs were extremely delicate and twisted.

Summary of Pathologic Findings: Examination revealed: The heart, normal; lungs, chronic passive congestion, emphysema, xanthic change, focal lymphoid hyperplasia; liver, biliary cirrhosis, xanthic change (local massive and diffuse), granuloma of undetermined cause, arteriosclerosis; kidney, passive congestion;

11. MacDonagh, J. E. R.: Naevo-Xantho-Endothelioma, Brit. J. Dermat. **24**:85, 1912. Congenital Xanthoma (Endothelioma), ibid. **23**:115, 1911.

ureters, moderate dilatation (hydro-ureter); spleen, passive congestion; pancreas, hypertrophy; suprarenals, atrophy; stomach and intestines, normal; skull, multiple xanthoma tuberosum with erosion; skin, xanthoma tuberosum; brain, xanthoma tuberosum (pineal, pituitary, tuber cinereum); spinal cord, normal; lymph nodes, hyperplasia, hemolymph nodes; jaundice; ascites.

Interpretation of Morbid Findings.—A general systemic chronic inflammatory process had manifested itself in a diffuse fashion on the liver and lungs, and in local nodular form in the brain, cranium and liver, very much as the disease

Fig. 22 (Case 2).—Skin lesion; tremendously vascular portion suggesting capillary nevus

gout may make its impress in different ways. The principal pathologic product of the basic disease process was fibrous tissue, together with its frequent companion the round cell infiltrate. The location at which two of these lesions occurred, the hilus of the liver and brain, accounts for most of the outstanding symptoms. The latter accounts for the polyuria which is the cause of the polydipsia. The hilum lesion explains the jaundice, biliary hypertrophic cirrhosis, and indirectly the hypercholesterolemia and widespread xanthic change. There remain thus few symptoms to associate directly with the individual basic disease in this patient, and which might be useful in distinguishing it from

others. The ones that appeal to us are the "diabetic" type of xanthoma lesion in a nondiabetic subject and perhaps the age of the patient and the involvement of the skull. So far as we can deduce from this case, the basic process in this child's disease may have been either a metabolic dyscrasia producing abnormal metabolites, or a low grade infection similar to tuberculosis or syphilis; this leads us nowhere.

GENERAL PATHOLOGIC CONSIDERATIONS OF XANTHOMA TUBEROSUM

Under this heading we must limit our discussion to certain selected phases of xanthoma pathology on which our cases have a particular bearing, for it would not be fitting or practical to essay a systematic and comprehensive consideration in this paper.

Nature of Fats Concerned.—In sections from four different xanthoma tuberosum cases we have been able to demonstrate all of the fatty groups which are susceptible to such determinations (neutral fats, soaps, cholesterol and myelins). All of these bodies have not been demonstrated in every case of xanthoma reported—cholesterol has been infrequently reported on the basis of histologic examinations, but on chemical analysis of lesions it appears to be constant. (It should be recalled that cholesterol exists amorphously as well as in crystalline form.) Neutral fats appear constantly. They are readily demonstrated by Sudan III and scharlach R, but usually not by osmic acid, that is, they are not the glyceroles of such unsaturated fatty acids as the oleates of normal human fats. We wish to call attention to a point already brought out by Pinkus and Pick [12] that globules of fat in these lesions which were originally spheroid may change to short crystals after preservation in solution of formaldehyd; that is, these crystals are artefacts. We have had the same experience; we have also found that the same transformation occurs in fatty changes in the kidneys. Unless informed, these crystalline forms are calculated to confuse the investigator.

We demonstrated soaps histologically in our cases by Klotz's method.[5] In our hands, the Nile blue sulphate method of Lorrain Smith for fatty acids was not adequate, for although we obtained granules which stained properly for the soaps, we did not obtain clear-cut differences in the staining controls of chemically pure soaps and fatty acids. From a knowledge of what happens in foci of low vitality in general, including necrosis, we consider it probable that all of these fatty bodies would occur in the older xanthoma lesions. From this, the valid fatty data (representative of the basic process) should be represented in early lesions only.

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12. Pinkus and Pick: Zur Struktur und Genese des symptomatischen Xanthoma, Deutsch. med. Wchnschr. No. 34, 1426, 1908. Löhlein, Virchow's Arch. f. path. Anat., **1**:180, 1905.

Kinds of Tissue Susceptible to Xanthic Change.—For the time being we will assume the definition of "xanthic change" to be "the abnormal presence of fatty bodies within cells in connection with xanthomatous tumors," thus using the latter term in its broad present-day acceptation. This takes no heed of the cellular process concerned, that is, whether the fat be present in the cell as the product of its own intracellular metabolic processes or simply as a matter of phagocytosis or imbibition. The future must give us the final information on these points, although we have good grounds for deduction today. Using the term in this sense, what kinds of tissue cells appear to be susceptible to this fatty process?

The white fibrous connective tissue cells are most susceptible. Those of the corium and the subcutaneous tissue, tendons, liver, lung and meninges have been found involved—those of the skin most commonly, those of the tendons frequently and the remainder rarely. Osseous tissue should not be included—in our case it was the tissue which was substituting for the cranial bone that became xanthic. We find no records of involvement of the congener connective tissues—adipose, cartilage, bone, etc. Under this heading may be included also the endothelial and lymphoid cells, both of which deserve further discussion.

As to endothelium, several workers believe that it shares in the xanthic change, as well as the spindle cells. Theoretically there can be no objection to this in view of the actively phagocytic properties native in endothelium, and the abundance of endothelium in the perivascular lymphatic spaces in which the xanthic change is known to concentrate. Coming to direct evidence, some authors state that they have seen the fat within endothelial cells, but it requires fine discrimination to distinguish an endothelial cell from a spindle cell per se once the cell has become swollen, as it does when it becomes phagocytic and loaded with fat. Positive conclusions should await the demonstration that the cell in question is part of the lining of some endothelial lined space. Essaying this, we have scrutinized the *lining* cells of the larger blood vessels in xanthomas, and even when their mantles were severely xanthic have found them unaffected. But in the case of the smaller vessels of the tuber cinereum, we have frequently seen the red globules (Sudan III preparations) there. In our xanthoma planum sections, the fibrous bundles were so sharply outlined that we can state that there were no endothelial cells concerned in the xanthosis there. It may be different when the cells are steeping in a less freely circulating medium and one perhaps with a different lipoidal content, such as is the case with extravascular endothelium. On the whole, we feel that the endothelial cells, even when they are separate from the blood vessel linings, may and frequently do contain the lipoids as well as the spindle cells.

Since lymphoid (and plasma) cells have propensities similar to those of spindle cells, we might predicate similar xanthic powers for them, but as a matter of fact they have little or no importance in the process. In cutaneous xanthomas these cells are not numerous, but in Dr. E. A. Shumway's eyelid sections which we studied and in the visceral lesions of our second case, they were numerous enough, yet never xanthic.

As to epithelium, Pollitzer [13] has observed a xanthic change in the nails, but he has made no microscopic report. Fat has been reported repeatedly in the basal layers of the epiderm, limited however to the surface just over the lesion of the corium. The crossed Nicol prisms bring these fats out splendidly. The cells thus affected do not swell at all as compared to those of the connective tissue; they would not be recognized individually as "xanthoma cells" and would receive little attention were they not associated with xanthoma. It appears to be the consensus of opinion that the fat in them is phagocytized, just as blood pigment appears in the same position over hemangiomas and other hemic dermatoses. But under these circumstances the epithelial cells are not hyperplastic; that is, their included fats are incapable of provoking a hyperplasia such as is ascribed to them in connection with the perivascular xanthoma cells. On this basis and because of changes taking place in the analogous and better studied fatty metamorphoses, we are inclined to disagree with Pollitzer in the minor matter of sequence of fat and cells in xanthoma. Pollitzer and Wile [1] believe that the fat is primary and provokes the cellular hyperplasia. We believe that the cellular hyperplasia often is primary, or at least basic—the result of various disease processes—and that the fat simultaneously at least, if not later, appears in the cell. It is probably deposited from the blood stream, but we hesitate to state this dogmatically in view of the involved pros and cons attached to the carefully considered subjects of fatty infiltration and fatty degeneration.

We have seen a marked fatty change in the arrectores pilorum muscles in two cases of xanthoma. The muscle cells do not assume the rounded form of the familiar "xanthoma cells," but remain as closely packed though swollen, elongated but rarified (hematoxylin and eosin sections) spindles with pyknotic nuclei. In Sudan III preparations such bundles are as conspicuously xanthic as any part of the lesion, and in point of bulk we would estimate that such a muscle bundle would consist of as much as 80 per cent. of fat.

We have not found any examples of skeletal muscle involvement in our material. It is not too much to expect that it might occur after

13. Pollitzer, S.: Discussion of Ravitch-Xanthoma tuberosum multiplex hypertrophicus, J. Cutan. Dis. **36**:303, 1918.

what we have seen in the involuntary muscle, but thus far Pollitzer appears to have been the only one to find such changes in the xanthoma planum cases.

Case 2 appears to be the only one exhibiting changes in nerve tissue, and as already stated, the gross changes were referable more to a xanthic change of fibrous tissue (meningeal fibroses extending into nervous tissue) than to involvement of the nervous elements themselves. We examined ganglionic nerve cells in the tuber cinereum sections and peripheral nerve trunks in the skin sections without finding them xanthic. Glia cells we did find degenerate and evidently xanthic, as brought out in the foregoing histologic descriptions. On the whole,

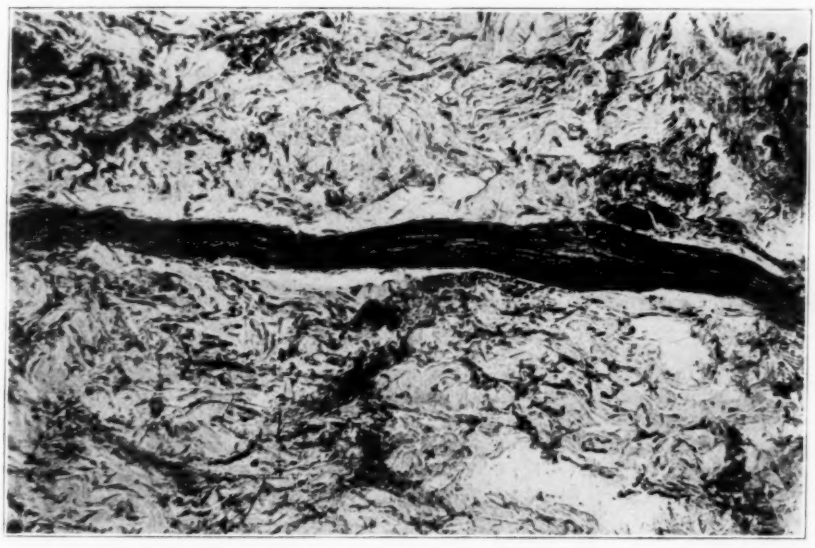

Fig. 23.—Xanthic arrectores pilorum muscle from skin of buttock (Case 1) Sudan III preparation, the black parts of the illustration being red in the section.

we must consider nervous tissue as being refractory to xanthic change just as it is immune to fatty infiltration even in cases of extreme obesity. Local xanthic change was recently found by Globus [14] in connection with a teratoid cyst of the hypophyseal region. This he interpreted as an incomplete development of sebaceous gland cells, a position quite untenable in view of his excellent photomicrographs. Apparently this xanthic change was occurring in nerve tissue, but the data are insufficient to prove that nerve tissue and not fibrous tissue was affected. A local cholesterol infiltration is quite under-

14. Globus, J. H.: Teratoid Cyst of the Hypophysis, Arch. Neurol. & Psychiat. **9**:417 (April) 1923.

standable in proximity to a focus which contains as much decomposing fatty material as does a teratoid cyst; we have seen it adjacent to a chalazion.

Cellular Pathology of Xanthic Processes.—We limit ourselves here to the rather academic question as to whether the lipoidal cellular changes are a "degeneration" or "infiltration;" that is, to but one phase of the cellular pathology. This raises moot points similar to those which have led some authors to avoid these two terms when discussing the comparable changes in which the neutral fats are concerned. "Fatty metamorphosis" is their refuge. As viewed today, the fats which we see in "fatty degenerated" cells may have had their origin either in those cells as the result of intracellular metabolic activities, or such fat may have been taken into the cells as fat from the blood; that is, in a fatty degenerated cell some of the fats have been proved to have "infiltrated." The essential idea of a fatty degeneration is thus that these fatty processes are taking place in a cell that is degenerate. If the fat deposit is taking place in a cell that is otherwise normal, it is a fatty infiltration.[15]

Applying these ideas to the cholesterol deposits, the first requirement is to determine whether the xanthoma cell is normal or regressive. Judgment here must be based largely on the state of the nucleus. Our personal opinion is that histologically the cell is not degenerate when it first becomes xanthic; that is, it is an infiltration so far as the original basic disease process is concerned. While the cell still maintains its fusiform shape (and yet contains fatty globules) its nucleus will have the reticular qualities of a hyperplastic cell — not a degenerate one. In the later stages, the small, spherical, pyknotic nucleus can in no way be construed as being that of a normal cell. It is degenerate, but this degeneration is a secondary development. Similar changes are seen in the fatty infiltration of liver cells, the signet of the well-known "seal-ring cell" representing the flattened, pyknotic nucleus of what is now really a degenerate cell.

In terms of general pathology, then, we consider xanthic change as basically a lipoidal and fatty infiltration of white fibrous tissue cells preeminently, but also affecting epithelium, muscle and nerve tissue.

Parts of Body Affected by Xanthoma.—If we except instances of atheroma such as Low [14] described, which are frequent in both natural and experimental blood cholesterol saturations, it is probable that our Case 2 is the only one reported in which there were found at necropsy

15. Adami, J. G.: Principles of Pathology, in General Pathology, ed. 2, Philadelphia, Lea & Febiger **1**:20, 1910.

visceral xanthomas in addition to the cutaneous ones. Krogius,[16] under the heading of "Xanthosarcomas in Tendon Sheaths," has cited Tourneux[17] as though metastases had occurred in the liver and lungs. On referring to the original articles which Tourneux cites (Billroth, Bolognesi, cases scattered through the *Beitrage zur Klinischen Chirurgie*, and Gaudiani), we find that metastases other than regional lymphatic ones were described only by Gaudiani, and that this one was of the skull. Furthermore, xanthoma cells were not described in any case, nor anything that might be interpreted as related to a xanthoma cell. We surmise that the designation "xantho" applies to a yellow color which was seen grossly, and which was referable to fatty degenerations and blood pigmentations.

We thus feel that these cases may be disregarded in relation to visceral metastases. In one other case than our own were the bones affected, as disclosed by roentgenograms (MacLeod);[18] but the irregularities of the wrist bones were referable to egg sized tumors in the soft parts, and not to lesions of the bones themselves.

Basic Diseases Concerned in Xanthic Changes.—Pollitzer was among the first to emphasize the systemic nature of xanthoma, pointing out its relation to rheumatism, diabetes mellitus and liver disease, and even today the list of definite diseases behind the xanthic smoke screen has become no longer. Diabetes mellitus and liver disease stand foremost, with rheumatism unconfirmed. But there are rumblings of others. Thus Broders'[19] consideration of seventeen xanthic swellings of the extremities led him to believe that the yellowing process occurred in old traumatic foci. Singularly, he makes no mention of blood cholesterol relationship. While in this connection in our own Case 2 there was a history of trauma of the skull, there were enough other circumstances to eliminate the simple traumatic factor in causation, such as the presence of visceral lesions and the histology. Another report to the point is that of Krogius,[16] who contends that the tendon sheath tumors are not the innocent affairs they are commonly thought to be, and he adduces the occasional "metastases" to internal organs as evidence. According to him, they are sarcomas showing a xanthic change. He is evidently considering the solitary lesions, and not xanthoma

16. Krogius, A.: Xanthoasarcomas in Tendon Sheaths, Finska Läkaresällskapets Handlingar **64**:102 (March-April) 1922; abst., J. A. M. A. **79**:173 (July 8) 1922.

17. Tourneux, J. R.: Sarcoma of Tendon Sheaths, Rev. de Chirurg. **47**:825, 1913.

18. MacLeod, J. M. H.: Brit. J. Dermat. **25**:349, 1913.

19. Broders, A. C.: Benign Xanthic Extraperiosteal Tumor of the Extremities Containing Foreign Body Giant Cells. Collected Papers by the Mayo Clinic, Philadelphia, W. B. Saunders Company **11**:1302, 1919.

tuberosum multiplex. Seyler [20] analyzed ten "solitary" xanthomas and concluded that three were valid neoplasms (blastoma), three were granulomas, and four were "apparently" granulomas; but the cause or even the estimated nature of the cause of the granulomas is not given. The granulomas of our Case 2 do not fit in with any of the previously described xanthic cases so far as the liver and skull lesions are concerned. We have already discussed (and fruitlessly) the nature of the basic granuloma in our case.

SUMMARY

Case 1.—Besides adding another case of tendon involvement to the list, this case shows that a plane and a tuberous lesion of the lid may be of the same nature—the same disease. While this does not prove that clinical xanthoma planum and tuberosum are the same disease, it strengthens the case materially; for, expressed in another way, this case at least shows to what extent the lesions of one and the same fatty dyscrasia may differ in appearance. By the same token, peculiarities in anatomy or physiology are not of themselves sufficient to explain the difference in morphology of plane lesions of the lid and tuberous ones elsewhere; other factors must be operative

Case 2.—Xanthic lesions, besides being numerous in the skin, were found in the lungs, liver, skull and brain. The presence of "xanthomas" in the viscera in this case is to be accounted for on the basis of coincidence, one moiety being the granulomas of an undiagnosed disease and the other a hypercholesterolemia.

The skin lesions were radically different from the visceral ones and were probably secondary to the hypercholesterolemia, which in its turn was induced by the systemic chronic inflammatory disease. Skin lesions showed none of the granulomatous characters which those of the liver and cranium did.

The skin lesions may have some diagnostic value in relation to this basic systemic disease by reason of their inflammatory (diabetic) character in a nondiabetic patient.

We report for the first time cholesterol within the white fibrous tissue bundles and xanthic changes in the arrectores pilorum muscles and in glia cells.

Xanthic or lipoidal infiltration should be included in the list of simple retrograde pathologic processes of the general pathologist. It is better to do this than to regard it as a variety of fatty infiltration. There are probably local as well as general xanthic states, but this

20. Seyler: Xanthomatous Granuloma, Virchow's Arch. f. path. Anat. **239**: 20 (Sept.) 1922.

remains to be proved in view of the lack of sufficient blood cholesterol determinations in connection with the local cases which have thus far been reported.

ADDENDUM

Since this paper went to press, Beeson and Albrecht [21] have reviewed the literature. They list extracutaneous xanthomas other than we have quoted as follows: (1) xanthomatous involvement of the dura mater associated with Hanot's cirrhosis necropsy proved and generalized tuberculosis. Visceral lesions were not mentioned. There are no records that the viscera were examined microscopically (Pinkus and Pick). (2) Bone destruction, in places cystic, as shown by roentgenograms (Merrill). (3) Involvement of cornea and larynx (Pusey and Johnstone). (4) A mass diagnosed roentgenologically at the spleen and heart (Knowles and Fisher).

DISCUSSION

DR. FRED WISE, New York: Dr. Weidman's paper shows the enormous significance of a knowledge of internal medicine in relation to diseases of the skin. To us the interesting parts of the paper are the new discoveries. In his last paper, Pollitzer claimed that xanthoma of the eyelids is due to degeneration of the muscle fibers alone, whereas in this paper that statement is denied. Probably, therefore, in some cases, as Weidman has pointed out, Pollitzer's contention is the correct one, but there are other cases in which degeneration of the muscle fibers has nothing to do with the disorder.

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21. Beeson, B. B., and Albrecht, P. G.: A Contribution to the Study of Xanthoma Tuberosum, with Report of a Case, Arch. Dermat. & Syph. **8**:695 (Nov.) 1923. The Knowles-Fisher reference should read as of 1921 instead of 1923.

NEWER PHYSIOLOGY OF THE SKIN

WITH SPECIAL REFERENCE TO THE ACTION OF ULTRAVIOLET LIGHT *

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The study of the functions of the skin is fundamentally a most complex problem. We are dealing with an organ spread out in a thin sheet over a large area with an extremely compact arrangement of heterogeneous elements. Metzner [1] has rightly said: "The many-sidedness of the tasks which every section of the skin has to fulfill brings it about that in this thin covering the most varied apparatus are crowded together and interwoven with one another in the smallest space, a circumstance which naturally makes very much more difficult the clearing up of the mechanism participating in the individual functions." The elemental processes of the skin are founded on the intricate mechanism of cell metabolism, with its innumerable checks and balances, and its responses to a multitude of diverse, almost infinitesimal stimuli. These are biochemical problems to be solved by studies in the borderland of both physiology and chemistry, and it seems reasonable that careful research in such methods will contribute valuable aid in the solution of the etiology of some of our diseases. An examination of the literature with reference to such studies brings out most decidedly the paucity of articles relating to exact scientific study of the skin's function. There are articles without number containing careful, minute descriptions of gross and microscopic appearances of diseases of the skin; there are likewise studies in focal infection, in internal secretion, in the relation of food and drugs, and in the relation of blood and urine conditions to skin disease, etc.; but there are few similar careful studies of the fundamental actions which occur in the pathologic conditions of the outer 2 or 3 mm. of our body.

SECRETION OF SWEAT

With a view to stimulating greater interest in the study of the functional activity of the skin, I wish to review briefly certain newer physiologic studies which give promise of adding much to the knowledge of

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* Read at the Forty-Sixth Annual Meeting of the American Dermatological Association, Ann Arbor, Mich., June 7-9, 1923.

1. Metzner: Lehrbuch der Physiologie des Menschen, Leipzig, 1920.

the various activities of the skin both in health and in disease. In the first place, there have been several studies on the secretion of sweat, especially with reference to the hydrogen-ion concentration. In two series of experiments, in 1919 and 1922, Talbert [2] found that the sweat secreted under the same environmental conditions, caused by either work or heat, had the same hydrogen-ion concentration. He found that the sweat from either of these factors was acid and was probably always so in health. His average in these cases was p_H 5.6. The sweat from skin covered with a rubber jacket yielded a higher hydrogen-ion concentration. This could be due either to carbon dioxid or to the volatile organic acids. But there was no increase in the carbon dioxid in the sweat of covered regions, and there was not the opportunity for the free escape of the organic acids, so that the latter were probably the cause of the higher p_H. There was also a regional variation in the amount of acid eliminated by the sweat glands, being distinctly higher on the leg, less on the arm and chest, and the least concentration occurring on the uncovered face.

In a more recent series of experiments he found that there was a greater amount of ash in the sweat produced by heat than in the work sweat, and that there was a greater amount of ash from the sweat of covered parts than from the sweat of uncovered areas, as well as a regional variation in these same parts. It is interesting to note that the parts of the body which eliminate the most acid yielded the smallest ash. He believes that the concentration of salts in the sweat glands is part of the function of these glands, and the higher the skin temperature the greater is the concentration.

A little later Leake,[3] in a determination of the occurrence of citric acid in sweat, determined by two methods that there was a substance which we are justified in believing to be citric acid in both the heat sweat and the work sweat. These observations also confirm Talbert's [2] in the fact that the human sweat is acid, their hydrogen-ion concentrations averaging 6.6.

In the normal cases studied by Pemberton and Crouter,[4] an average initial reaction of the forehead sweat corresponds to a p_H of 7, which is just on the acid side of the blood reaction. They state that the reaction of sweat at various sites may vary, but further work is needed to

2. Talbert, G. A.: Effect of Work and Heat on the Hydrogen Ion Concentration of the Sweat, Am. J. Physiol. **50**:433 (Dec.) 1919. Further Studies on the Hydrogen Ion Concentration of Human Sweat, Ibid. **61**:493 (Aug.) 1922. Ash of Human Sweat Produced by Heat and Work, Ibid. **63**:350 (Jan.) 1923.

3. Leake, C. D.: The Occurrence of Citric Acid in Sweat, Am. J. Physiol. **63**:540 (Feb.) 1923.

4. Pemberton, R., and Crouter, C. Y.: The Response to the Therapeutic Application of External Heat, J. A. M. A. **80**:289 (Feb. 3) 1923.

elucidate this question. They also found that during the course of the therapeutic bake for arthritis there was a consistent and marked tendency for the reaction of the sweat to change toward the less acid or more alkaline range, irrespective of whether it was acid, neutral or alkaline at the outset. This tendency was invariable among normal persons and marked among persons with arthritis.

Still more recently Sharlit and Scheer,[5] in a series of hydrogen-ion concentration tests in eighty-five persons, found the hydrogen-ion concentration of the skin surface to be about 5.5. They also found that there is a mechanism in healthy skin for maintaining a constant p_H of its surface. They find reasons for believing that the keratin of the horny layer is the element which is giving this reaction.

The value of these experiments seems to me to lie in the fact that the sweat is definitely proved to be acid, after the many controversial statements which have appeared in the literature in the past. The second point of importance is the definite regional variation in the acidity and the amount of ash. It seems reasonable to expect that further experiments of this sort will throw light on the predilection of certain diseases for certain areas of the body, and furthermore may give additional information in regard to the occurrence of diseases in patches over various parts of the body. I feel that we can look to similar work of this character for notable contributions to our knowledge of etiologic factors of skin diseases.

ACTION OF CAPILLARIES OF THE SKIN

The action of the capillaries of the skin has been a subject of increased study in the past few years. The development by Lombard[6] of a more satisfactory method of observing capillary activity has been the means of obtaining valuable data. Such work has shown that the superficial capillaries respond both to chemical and nerve influences, and that the capillaries and the tiny veins function actively as well as the arterioles. Of particular importance has been the work of Carrier.[7] He has examined the rate of flow, the character of the stream and the state of the capillaries under various stimuli. He used different chemicals, mechanical irritation and changes in temperature, and observed the varying effects under the microscope. Cold produced a contraction of the arterioles with a slowing of the blood stream and contraction of the

5. Sharlit, H., and Scheer, M.: The Hydrogen-Ion Concentration of the Surface of the Healthy Intact Skin, Arch. Dermat. & Syph. **7**:592 (May) 1923.

6. Lombard: The Blood Pressure in the Arterioles, Capillaries and Small Veins of the Human Skin, Am. J. Physiol. **29**:335, 1912.

7. Carrier, E. B.: Studies on Physiology of Capillaries. V. Reaction of Human Skin Capillaries to Drugs and Other Stimuli, Am. J. Physiol. **61**:528 (Aug.) 1922.

capillary wall. Using various drugs—epinephrin, histamin, pituitary extract, amyl nitrite, etc.—he demonstrated that the local application showed that the capillaries had the power of independently contracting or relaxing. Mechanical irritation likewise, stroking for example with a blunt point, opened all the underlying vessels. He asserts that it is possible that dermographism may be due to direct mechanical stimulation and not as much to the action of the sympathetic nervous system as has been thought. Thus it would seem that the diameter of the capillaries is not necessarily dependent on the pressure in the arterioles, but rather on their own tone and state of contraction. They normally contract or relax independently of the pressure behind them, but in response to local or general stimuli.

Michael,[8] Boas [9] and others have studied the capillary loops and their actions in various pathologic conditions, but more study is needed to place properly the value of this technic. Again, it is not unreasonable to assume that further studies may give us still more information relative to the occurrence and cause of some of the patchy diseases of the skin.

ATROPHY AND AUTOLYSIS OF TISSUE

Bradley [10] has pointed out further evidence of physiologic activity in the skin. In discussing the subject of atrophy and of autolysis or self-digestion of tissue, he states that there is evidence of two groups of enzymes in tissue—one acting only in acid mediums and converting the acid tissue proteins into primary cleavage products; and a second one which attacks only the primary cleavage products of proteins producing the amino-acids. Any increase in acid production in cell or tissue beyond the capacity of the buffer mechanism to dispose of immediately must automatically tend to atrophic changes; or if the production is in sufficient amount, the process will go on to complete destruction. He quotes as the most striking example of this process the work of Marshall [11] in connection with "mustard gas." Briefly summarized, this process is as follows: This gas penetrates the skin by virtue of its organo-solubilities and becomes concentrated in both the water and lipoid phases. There is hydrolysis, with the consequent

8. Michael, J. C.: Dermatoscopy, Arch. Dermat. & Syph. **6**:167 (Aug.) 1922.

9. Boas, E. P., and Frant, S.: The Capillary Blood Pressure in Arterial Hypertension, Arch. Int. Med. **30**:40 (July) 1922.

10. Bradley, H. C.: Autolysis and Atrophy, Physiolog. Rev. **2**:415 (July) 1922.

11. Marshall, E. K.; Lynch, and Smith, H. W.: On Mustard Gas: The Systemic Effects and Mechanism of Action, J. Pharmacol. & Exper. Therap. **12**:265 (Dec.) 1918. Marshall, E. K.: Mustard Gas, J. A. M. A. **73**:684 (Aug. 30) 1919.

formation of hydrochloric acid. This process goes on slowly and starts the autolytic mechanism which kills the cell. The rapid blistering and necrosis after the process first becomes evident is an expression of the speed with which the autolysis goes on. By analogy it is not difficult to reason that milder effects, that is, the production of atrophy over widespread areas or in smaller scattered areas, might depend on a somewhat similar mechanism probably initiated from within the body.

ACTION OF ULTRAVIOLET LIGHT ON SKIN

The most important physiologic studies on the skin in recent years have been concerned with the action of ultraviolet light. There has been much experimental work on this subject, and numerous facts are being accumulated, interpreted, and correlated, but our knowledge is still limited. From the clinical point of view the effect on the skin varies with the distance of the source of the light from the skin, the time of exposure, and the voltage employed, as well as with the type of skin and the location of the body which is treated. Evidence is accumulating which indicates that the amount and type of filtering material employed may vary the action of the light. Depending on the amount of the dosage, there will be only a transitory erythema, or a more intense erythema with considerable burning sensation, followed by a varying amount of desquamation. A larger dose will produce an intense exudation of serum, as shown by the vesication or large bullae produced, with considerable crusting and exfoliation. There may be great discomfort, or even pain enough to produce actual disability, to say nothing of the irritation of the eyes which may result if they are not properly protected. Later, pigmentation will follow, either from a large dose or by the use of repeated smaller doses, without the appearance of anything more than a transitory erythema.

Physiologically speaking, it is possible to produce a temporary vasodilatation, probably by direct action of the light on the cells of the capillary walls. It is also possible to carry this effect to the point where there is an increased permeability of the vessel walls. There is an increased desquamation, perhaps by an acceleration of the keratinization process. There is also an increase in the production of pigment of the basal layer of most skins. There is also evidence of increased hair growth, probably resulting from the increased vasodilatation, and also evidence of some decrease in the activity of the oil glands, perhaps by reason of the rapidity of exfoliation.

Biologically, the exact action is a problem of some complexity. The effect of the ultraviolet light is thought by Clark [12] to be due to a photo-

12. Clark, J. H.: The Physiological Action of Light, Physiolog. Rev. **2**:277 (April) 1922.

chemical reaction produced when the light energy is absorbed. Harris and Hoyt [13] carry it a little further and think that the toxic action of ultraviolet light is due to absorption of rays by certain constituents of all living protoplasm, namely, the tyrosin and phenylalanin radicals of protein molecules. Various experiments have shown that protein solutions are made less soluble by ultraviolet light; that lipoids are more soluble; that egg albumin can be changed to act like globulins; that oxygen becomes converted to zone, etc. The lethal effect of ultraviolet light on micro-organisms has been known for a long time. It has been found, within certain limits, that the shorter the wave length the greater is the lethal effect; that wave lengths of 2,960 Ångström units or less, at 37 C., were more effective than longer wave lengths; but that at higher temperatures the longer wave lengths were lethal. Bovie [14] has shown, in experiments on paramecia, that sublethal doses make them so sensitized to heat that after exposure to ultraviolet light they will not tolerate the usual optimum temperature for one minute; and furthermore that a sublethal dose inhibits cell division. These brief statements of results are examples of data which are being obtained. These data need to be correlated and interpreted, to say nothing of the additional work needed, in order to formulate a definite knowledge of the fundamental action of light on the skin.

There has been much discussion in regard to the penetration of the skin by these rays. Hasselbach,[15] as quoted by Clark,[12] gives the following table:

Transmission of Light by the Skin

	Wave Length ($\mu\mu$)							
	436	405	366	334	313	302	297	280
Per cent. transmitted by skin 0.1 mm. thick	59	55	49	42	30	8	2	0.01
Per cent. transmitted by skin 1.0 mm. thick	0.5	0.3	0.08	0.02				

The shorter the wave length, therefore, the thinner the layer that will absorb them. Thus the wave lengths from 4,360 Ångström units to 3,000 Ångström units are relatively more penetrating, and the rays below 3,000 Ångström units are absorbed by the epidermis in a layer 0.1 mm. thick. It has been shown that these shorter wave lengths have almost no effect on pigmentation, perhaps because of their inability to penetrate to the basal layer.

In this connection some one has called attention to the relation between this decrease of penetrability with diminution in wave length and the decrease in penetrability in the case of roentgen rays but with

13. Harris, F. I., and Hoyt, H. S.: The Possible Origin of the Toxicity of Ultraviolet Light, Science **46**:318, 1917.

14. Bovie, W. T., and Klein, A.: Jour. Gen. Physiol. **1**:331, 1918.

15. Hasselbach, K. A.: Biochem. Ztschr. **19**:435, 1909.

an increase of wave length, so that above the longest roentgen rays and below the shortest ultraviolet rays it would seem that there is apparently a zone of wave lengths with practically no power to penetrate, about which we know nothing at the present time.

Further relationship of light to physiologic processes of the skin is shown in other ways. Hematoporphyrin has been found to be an active sensitizer to light for higher animals. The unfortunate condition of Meyer-Betz [16] produced by the injection of hematoporphyrin into his own blood, and the finding of hematoporphyrin in the urine in the cases of hydroa, are examples of the sensitization of the cells of the skin to light. The occurrence of pellagra lesions is an example of a similar condition. LeRoy and Pacini [17] have produced lesions in pellagrins by ultraviolet light from magnesium. Corn meal and pellagra have been associated for a long time. The glutelin of corn has a high percentage of tyrosin as compared to other proteins. It is suggested that tyrosin photosensitization of the skin may be the factor in this disease. The work of Harris and Hoyt [13] suggests that the amino-acids, tyrosin and phenylalanin, impart photosensitivity to the protein of which they are a part. It might be inferred that this photosensitivity is in proportion to the amount of the amino-acids in the particular protein. Food may therefore play a larger part in this process, as is already suggested by studies on pellagra and rickets.

The pigmentation of the skin produced by ultraviolet light is undoubtedly an important factor. Bloch [18] and his collaborators have shown that the cells of the germinative layer, of the outer root sheath and of the hair matrix form a pigment in their plasma. These cells form an oxidizing ferment, and the pigment is produced by the action of this ferment on some substance which is brought to the cell by the blood stream. He also shows that the skin of albinos and the white parts of the skin of spotted animals are without this ferment. An increase in pigmentation is due to the fact that this process of pigment manufacture is hastened by various stimuli, and he suggests that the actinic effect of light depends on an increase of this ferment. The melanin which is formed is undoubtedly the end-product and is the result of the action of the oxidizing ferment. Rollier [12] is convinced that the beneficial action of sunlight is due to the pigmentation which is produced. It is possible that the chemical change taking place in the epidermal cells, resulting in the formation of pigment, acts in some way as a stimulus to metabolism. Rays above 3,300 Ångström units

16. Meyer-Betz, F.: Deutsch. Arch. f. klin. med. **112**:476, 1913.

17. Pacini, A. J.: Outline of Ultraviolet Therapy, Ed. 1, Chicago, Poole Bros., 1923, p. 179.

18. Bloch, B.: New Investigations Concerning the Problem of Cutaneous Pigmentation, Bull. Soc. franç. de dermat. et syph. **28**:R.S. 77, 1921.

and below 2,900 Ångström units produce little pigment. The lower wave lengths are apparently absorbed before they reach the basal cells of the epidermis and therefore could not be expected to be a factor. But whatever the effect of the pigment formation, it is evident that ultraviolet light has an action on internal organs. The beneficial effects obtained in tuberculosis and the brilliant work of Hess [19] and his co-workers in connection with rickets are well known. Further evidence of the influence of the ultraviolet light on body metabolism is given by the results which show a change in the amount of the carbon dioxid expired, a change in the rate and depth of respiration, and increased rate of growth in light as compared to darkness. Most observers are agreed that ultraviolet light stimulates a lymphocytosis. Tisdall [20] has shown that the use of ultraviolet light in rickets has caused a marked increase in both the calcium and inorganic phosphate content of the blood serum. Levy [21] and Gassul [22] have shown that intensive radiation of the whole body surface will cause an intense engorgement of the spleen, lungs and liver. There is, then, not only the action on the skin, but an effect on distant organs, explained perhaps on the basis of a cutaneous reflex of some sort in much the manner that Head has connected surface pain with internal organs. This effect may be explained better by the assumption that some photochemical product formed at the surface is conveyed to the viscera by the blood. The hemorrhages occurring in patients with tuberculosis after exposure have resulted in the adoption of a graduated fractional dosage, and we will do well to adopt a similar program in the treatment of generalized dermatologic conditions.

It has also been pointed out that diabetic patients react poorly and give evidence of increased toxic distress, so that it will be a wise procedure to use extreme care in the ultraviolet treatment of patients with glycosuria.

Sampson [23] has called attention to certain observations which he has made over a period of four years in the combined use of the ultraviolet light and roentgen ray. He states that ultraviolet and roentgen-ray radiations are physiologic complements; that ultraviolet light applied

19. Hess, A. F., and Weinstock, M.: A Study of Light Waves in Their Relation to Rickets, J. A. M. A. **80**:687 (March 10) 1923. Hess, A. F.: Newer Aspects of the Rickets Problem, J. A. M. A. **78**:1177 (April 22) 1922.

20. Tisdall, F. F.: Effects of Ultraviolet Ray on Calcium and Inorganic Phosphate Content of Blood Serum of Rachitic Infants, Canad. M. A. J. **12**:536 (Aug.) 1922.

21. Levy, M.: Strahlentherapil **7**:602, 1916; **9**:618, 1919.

22. Gassul, R.: Strahlentherapie **10**:1162, 1920.

23. Sampson, C. M.: Ultraviolet and X-Ray as Physiologic Complements in Therapeusis: A Newly Established Clinical Treatment, Am. J. Roentgenol. **9**:570-584 (Sept.) 1922.

first renders the area more resistant to subsequent roentgen-ray radiation; that the roentgen ray applied first may produce a dermatologic change injurious to the organism, but the effects of that injury can be alleviated or entirely neutralized by applying secondarily the ultraviolet radiation. Working on this basis he reasons that ultraviolet light greatly extends the previous limits of roentgen-ray efficacy in the treatment of disease. Further confirmation of this work is needed.

In a paper of this sort I can do little more than hint at some of the clinical uses of ultraviolet light. The work of Finsen with lupus vulgaris is the classical example. Capillary nevi and roentgen-ray telangiectases are benefited by the application of pressure with the water-cooled lamp. In some cases of chronic eczema the itching, infiltration and redness will fade away rapidly with treatment. Some cases of acne do well, but I do not think the permanency of the results can be compared with those obtained with the roentgen ray. In granulating areas of various types it is often astonishing to note the rapidity with which they heal. The sinuses of tuberculous origin respond very well to treatment, much quicker results being obtained, I think, when generalized radiation as well as local is used. Certain cases of erythema induratum are amenable to ultraviolet light treatment. There have been many cases of alopecia areata reported in which this treatment has been a success. Recently it has been found that cases of pityriasis rosea are shortened and relieved of itching by a few treatments. The lesions in psoriasis are often affected to a marked degree, and the older lesions will disappear at times almost as fast as the more recent ones. In furunculosis, general systemic treatment is a valuable measure. Reports of its success in the treatment of other dermatoses are appearing constantly. It is not a cure-all by any means, and we are undoubtedly in a period of overenthusiasm in regard to its use, and many of the facts relative to its action and use are still a matter of conjecture. The fact remains, however, that ultraviolet light therapy has come to be a valuable method in the treatment of certain dermatologic conditions. With our increasing knowledge in regard to the action of light and the refinement of apparatus and technic, it will undoubtedly be found that certain wave lengths will have a more beneficial effect than others, or that certain of these beneficial wave lengths will have an effect on one disease and not on another. It also seems possible that an increasing use of filters will modify our technic to a certain degree.

SUMMARY

In conclusion, I wish to state that I have endeavored to emphasize the importance of knowledge of the fundamental physiologic processes of the skin. This brief survey of the more recent physiologic research work suggests:

1. That the elimination of acids in the sweat and the action of the capillaries of the skin, or both of these factors, may play some part in the occurrence of patchy diseases, or the predilection of certain diseases for certain areas of the body.

2. That the autolysis of cells may be the fundamental action in the production of atrophic areas.

3. That ultraviolet light has a distinct effect on cell metabolism, this effect being exerted not only locally on the skin, but on deeper organs and the general body metabolism as well.

Future research in this field of physiologic dermatology will undoubtedly result in a clearer insight into the exact nature of normal and pathologic activities of the skin. Such work is greatly needed, and this survey will have served its purpose if it calls attention to this need and stimulates a development of our knowledge of this subject.

DISCUSSION

Dr. John H. Stokes, Rochester, Minn.: May I take this opportunity to express a feeling of regret that so much of the fundamental physiologic work in our field is being done by other than dermatologists, especially in this country.[2] These contributions by physiologists and biochemists are being rapidly taken up by internists and vigorously applied to the study of the skin, while American dermatologists content themselves with purely clinical observations and speculations. It is to be hoped that we may soon restore the appropriate balance to our work and give to American dermatology the atmosphere of fundamental scientific distinction which has surrounded the work of many of our European confreres.

Dr. William Allen Pusey, Chicago: I would like to second the remarks of Dr. Stokes on the importance of papers of this sort. The editor of one of the most important Scandinavian journals recently had an article, partly facetious, on this subject and said that it would be a good plan if the medical journals closed their columns for the next five years to papers on new subjects and confined them to studies on things we know. I think Dr. Lane has performed a most useful function in giving us this paper and calling our attention to the need of reviewing what we already know. The papers of Sweitzer, Pardo-Costello and that of John Lane, which is to come, are simply cerebral irritants. You think you are nicely settled down to enjoy life and have things all classified and taken care of when somebody comes along with a "dermatitis innominata speculata," or something else like that, and you have to begin all over again. We have to get these new things, but dermatology is already a mass of material, and along with the new dermatoses we need widespread study and correlation and formulation of the knowledge we already have.

Dr. John E. Lane, New Haven: I wish to suggest that if possible Dr. Lane study the complementary action of the roentgen ray and ultraviolet ray as reported by Sampson. The complementary action as suggested by Dr. Sampson is interesting, but the claims of Dr. Sampson were to my mind in no way demonstrated by the experiments described in his paper. Further and more careful study will be necessary before any definite conclusions can be drawn in regard to this.

Dr. C. Guy Lane, Boston: On looking through the literature and preparing this paper I was impressed with the thought that Dr. Stokes has emphasized —that the greater part of the work is being done by men outside of dermatology—by physiologists, chemists, and others; and it would seem to me that we, as dermatologists, should participate more in this sort of research because of our knowledge of the skin and its diseases.

One other point comes to my mind in regard to the physiologic activities of the skin. The importance of its secretion was emphasized in an article on eczema in rubber workers, and mention was made of the different opinions existing as to whether the sweat was actually acid or not. The work of McConnell has also emphasized the secretion of the skin as a factor in dermatologic diseases in printers.

I think that Dr. John Lane was right in speaking of the work of Sampson. If that work is true and accurate, it is quite an important contribution to our dermatologic work, but it should be confirmed before being adopted for wide usage.

A CASE OF DIFFUSE SCLERODERMA PRESENTING UNUSUAL FEATURES

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The etiology and pathogenesis of the so-called idiopathic scleroses and atrophies of the skin is still such a mystery, and the classification is in many ways so unsatisfactory, that the record of a case which presents such a variety of symptoms as occurred in the patient about to be described may be of interest and perhaps of value.

REPORT OF A CASE

History.—E. G., an American girl, aged 12, was admitted to the New York Skin and Cancer Hospital on Oct. 26, 1922, with a diagnosis of scleroderma. The family history was negative for tuberculosis and syphilis. The patient had had scarlet fever when about 4 years of age, with uneventful recovery, and measles in May, 1918, when about 7½ years old. Soon after recovery from measles, the patient said, she had a sore mouth, involving the buccal and labial mucous membrane, and lasting about two weeks. This seems to have occurred at about the same time as the onset of the scleroderma, but the history was not quite clear on this point. There had been no stomatitis since.

She was admitted to the Presbyterian Hospital on July 9, 1918, under which date the following note appears: "Two weeks after recovery from measles mother noticed swelling on left knee and ankle. It hurts child to walk. When child wakes up, cannot put left heel to ground. Rash on same leg for six weeks." The provisional diagnosis was eczema. This account of the onset of the disease does not agree in all points with later statements by the patient, who said that the first symptom noted was a swelling on the inner surface of the left knee, with no change in color, and the appearance of a brownish spot on the left flank. The patient felt fatigued, and walking became progressively more difficult, as above noted; but at first there was temporary improvement in the afternoon. Examination at the Presbyterian Hospital showed the left knee somewhat swollen, being about 1 cm. larger than the right, the swelling being mostly over the inner aspect of the joint. There was some limitation of extension, but flexion seemed to be normal. There was no heat or tenderness. Measurements from the crest to the internal malleolus were the same on both sides, and there was no atrophy of the muscles of the thigh or leg. There was a dermatitis extending from the ankle to the groin along the inner aspect of the leg. This dermatitis is not described; presumably it was a band of pigmented sclerodermatous skin. The glands in the groin were enlarged, and a few epitrochlear glands were to be felt above the left elbow. The sharp edge of the spleen was palpable about 2 inches (5.08 cm.) below the costal margin. The patient said that there was soreness, but without ulceration, on the front of the left ankle about that time. A lateral roentgen-ray view, taken July 11, 1918, suggested an infusion into the synovial sac of the knee, but there was

no erosion or periostitis. The lateral posterior view seemed to be negative. The blood Wassermann test was negative. On discharge, Aug. 28, 1918, the only change noted was a reduction of the swelling of the knee.

She was next treated at the Vanderbilt Clinic, and in October, 1918, was presented at the Section on Dermatology of the Academy of Medicine. The disease was then described as "a slight erythema and scaling, extending from the dorsum of the left foot along the shin to the knee, which was slightly swollen. The skin over the dorsum of the left foot and shin was definitely hidebound."

The disease progressed slowly, and in the summer of 1919 an ulcer appeared in front of the left ankle, gradually spreading outward and backward nearly to the sole and the tendo Achillis, while the part of the ulcer in front of the joint gradually healed. This scar has not again broken down. Soon other ulcers appeared on the inner aspect of the left foot. In the summer of 1920, the disease appeared in the skin in front of the upper part of the right knee as a hard, hot, red, tender and painful patch. This condition gradually spread down the front of the knee and shin to the ankle. The patient said that first scabs formed on this inflamed skin, and then crusts, the removal of which revealed ulcers. This sequence corresponds exactly with my own observations of the development of the ulcers on the shin. About the same time, a book fell on the right great toe, leading to a painful inflammation and the loss of the nail, and a little later to the development of an ulcer which had persisted—sometimes better and sometimes worse. This traumatic origin of the ulcer seems to be more common in scleroderma than does the spontaneous development, which also was noted in this case.

On March 8, 1922, she was admitted to the Presbyterian Hospital, having been unable to walk for about three years. The distribution of the disease at that time is shown by the accompanying illustrations. On the trunk and the thighs there were areas of brownish pigmentation over thickened skin and subcutaneous tissue, while on the left leg and on both feet—but especially the left—were ulcers and foul-smelling purulent crusts. The left knee and ankle were ankylosed. There was no generalized adenopathy, although a large cervical gland was noted on each side, and the axillary glands were also palpable. The pharynx was injected, the tonsils large, the teeth irregular and irregularly set, the gums red, swollen and bleeding. No mention is made of any abnormality of the skin of the upper extremity. Blood examination revealed 96 per cent. hemoglobin; 10,200 white blood cells. The differential count revealed 53 per cent. polymorphonuclears, 44 per cent. lymphocytes, 2 per cent. transitionals and 1 per cent. eosinophils. Red blood cells and platelets were normal.

The Wassermann reaction was negative, both with alcoholic and with cholesterinized antigen.

Roentgen-ray examination showed definite evidence of calcification in the soft parts in the posterior portion of the right leg. The left leg showed beginning calcification. This was more suggestive, to quote the report, of ossifying myositis than of scleroderma. The bones of both legs were atrophied.

She remained in the hospital until May 27, 1922, there being little or no change during this time except that there was less odor in the discharge from the ulcers.

On Oct. 26, 1922, she was admitted to the New York Skin and Cancer Hospital, the condition beginning much as it did during the previous spring except that there was more foul-smelling discharge from the ulcers on account

of the impossibility of receiving adequate care at home. The Wassermann reaction was negative and the urine normal except for a faint trace of albumin.

Examination.—The skin showed a great variety of changes. On the face it was muddy and freckled, but nowhere thickened, and there was no atrophy or beaking of the nose. There was no atrophy of the subcutaneous tissue, the face being, on the contrary, rather full and round. On the left cheek, about

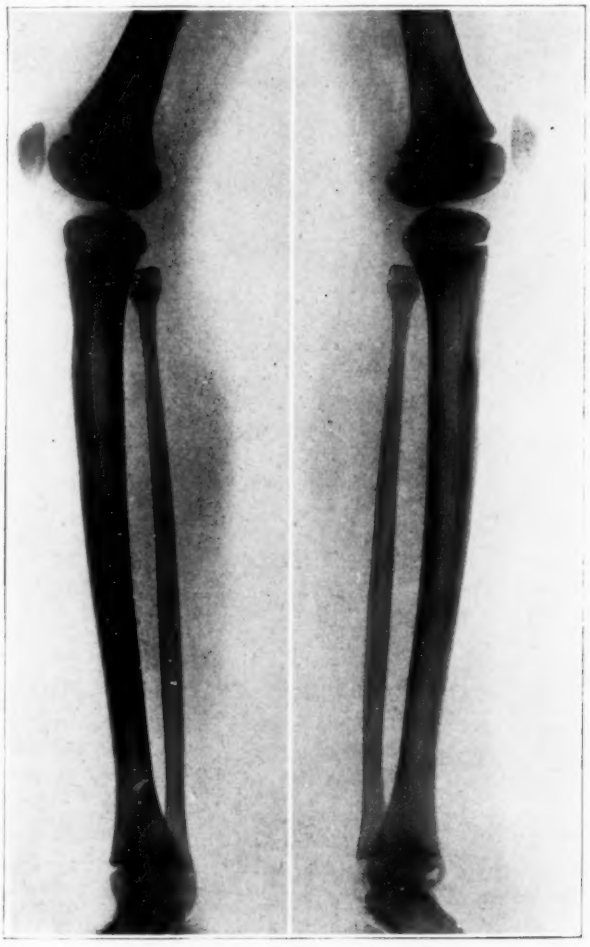

Fig. 1.—July, 1918: Right knee and leg, normal.

an inch and a half behind the angle of the mouth, there was an area about half an inch (1.27 cm.) in diameter in which there was a suggestion of atrophic pitting. On the front of the chest, the skin was thin and transparent, the veins showing through, but was normal in texture and color.

On the right flank, between the crest of the ilium and the ribs, there was an irregular pigmented area measuring about 2 by 4 inches (5.08 by 10.16 cm.), the long diameter running downward and forward. The border was irregular,

and beyond it there were scattered a number of erythematous spots about a sixteenth of an inch (1.5 mm.) in diameter, pale and scarcely visible. Some of these spots were slightly larger than the others and presented a slightly atrophic center having the color of early lineae albicantes. Throughout the patch the skin was slightly atrophic, though when pinched up between the fingers the difference in thickness between it and the adjacent normal skin was

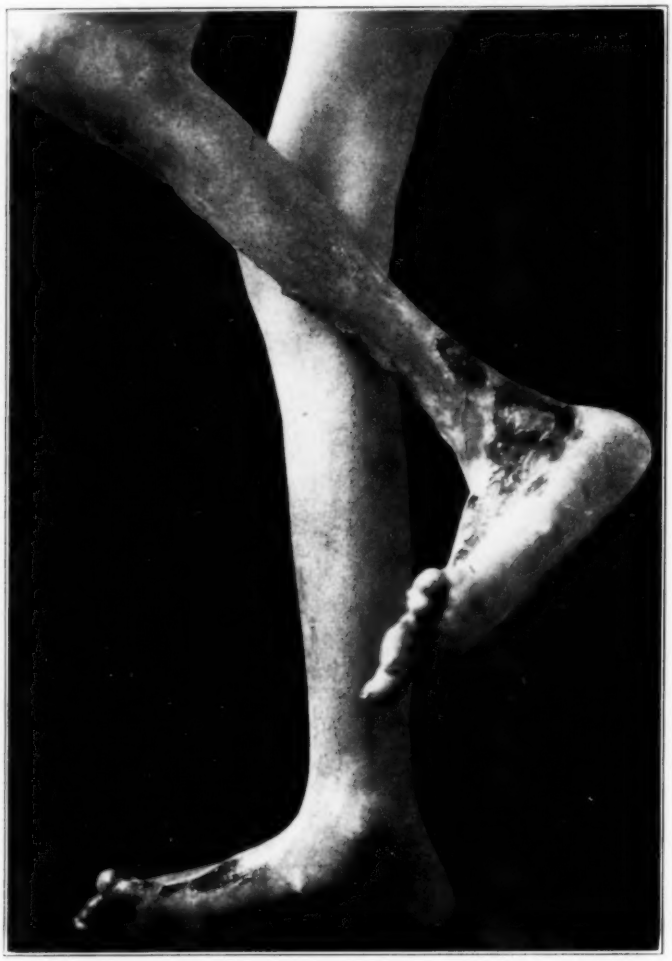

Fig. 2.—March 8, 1922: Mottling of skin, ulceration, ankylosis of knee and deformity of toes.

barely perceptible. The veins were more clearly visible, especially in the anterior third, than in the surrounding skin, and this part showed also a mottled brownish pigmentation, the mottlings being lighter in color than the network. This patch was said to have been present for three and a half years.

The left flank carried a similar patch, but much larger, extending from the tenth rib in the posterior axillary line to the midline for an inch below the umbilicus. The pigmentation here was much greater than on the right side and the atrophy in the center was further advanced, forming a white crinkly area about 1 by 2 inches (2.54 by 5.08 cm.). This patch had been present since the onset.

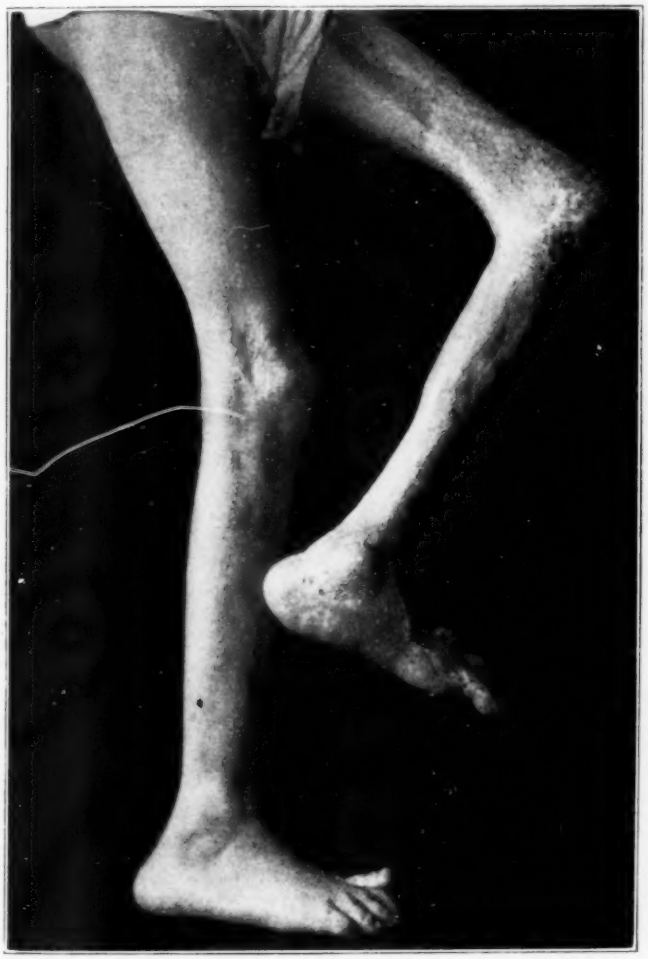

Fig. 3.—May 27, 1922: Hidebound skin around left knee, wrinkling of skin over right knee and atrophy of whole left lower limb.

The skin of the back was normal as far as the sacrum, except where the disease extended from the shoulders. On the left side this extension covered most of the scapular region with pale brownish pigmentation, dotted with spots of atrophy varying from one thirty-second of an inch in diameter to irregular blotches half an inch long, the smaller ones being pale lavender,

the larger ones white. Over the right scapula the disease was much less extensive, and there were no white areas. The skin behind and immediately below the right axilla was pinkish lavender, suggesting a toxic congestion, but no thickening could be felt.

Right Upper Extremity: The fingers were normal, there being no sign of clubbing, tapering, atrophy or sclerosis. The palm was normal. On the dorsum of the hand the veins were prominent and plainly visible and the skin

Fig. 4.—Jan. 16, 1923: Right foot, beginning atrophy in midtarsal region.

thin, but without evident general atrophy. There were many pale or white atrophic spots from a sixteenth to an eighth of an inch in diameter. The occurrence of these atrophic spots was continued in an indefinite band along the forearm to the external condyle and on to the posterior surface of the arm. Throughout this region the white spots were replaced by violaceous depressions. The skin covering the olecranon itself was normal or slightly roughened. The atrophy of the skin of the upper arm was bounded above by a sharply defined line extending from the posterior axillary fold just above the inner margin downward and forward to a point near the middle of the

inner aspect of the arm, where the line became vague but extended approximately horizontally forward to the anterior surface of the arm. This line was marked by a difference in color and in texture of the skin rather than by any change in thickness. The region behind it, extending over the external surface of the arm and on to the peak of the shoulder, was light brownish, almost violaceous, and dotted with small atrophic spots like those occurring on the hand and forearm. The anterior aspect of the arm and shoulder was approximately normal.

Fig. 5.—Jan. 16, 1923: Right knee, showing little change.

Left Upper Extremity: The skin on the left hand was like that on the right except that the atrophic spots were a little larger and more numerous. The left forearm also was like the right, except that the atrophic spots were more evenly distributed, although they still were more numerous on the radial surface. On the left arm the atrophy was rather more extensive than on the right, but hard to define. The only free areas were a triangle on the inner surface, extending about 3 inches (7.62 cm.) downward from the axilla and an area about an inch (2.54 cm.) broad at the base, extending horizontally across the anterior axillary fold and curving downward about 2 inches (5.08 cm.) on to the anterior surface of the arm.

From the foregoing description it will be seen that the greater part of both upper extremities was involved in an atrophic process, but there were no areas of hard skin, no bands or plaques, no crinkling, no adhesion to bone. In fact, the whole process here might easily be overlooked.

The condition on the lower extremities showed in places, as on parts of the thighs, the same changes as were seen on the arms, but in addition there were extensive sclerosis, atrophy and ulcerations.

Fig. 6.—Jan. 16, 1923: Atrophy and ankylosis throughout tarsus; calcification in tendo Achillis.

The left foot showed the greatest changes. An ulcer about an inch broad, forming the two sides of a right angle, had replaced the skin above and in front of the internal malleolus. On the outer aspect, the ulcerated surface extended from a point a little in front of the tendo Achillis forward along the outer border, curving upward on to the dorsum and reaching to and between the three outer toes; thence the ulcer continued backward on the sole under the third and fourth toes for about three-quarters of an inch (1.9 cm.). The ulcers were covered with thick brownish crusts, removal of which revealed a

pale base bathed in pale green pus. The crusts were adherent at the edges and removal was difficult and painful. There was no involvement of the great toe or of the second toe, while the skin of the other toes was crusted. The skin over the front of the left leg was thin, hard and adherent to the bone beneath. In the lower two-thirds there were several long narrow ulcers covered with dark crusts. These crusts were thinner and less frequent in the upper part, but a few were found even as far as the condyles. The thicker crusts covered ulcers, the thinner crusts seemed to rest on dry atrophic skin. The skin covering the patella, the condyles and the upper third of the shin was

Fig. 7.—Jan. 16, 1923: Left knee, showing atrophy and ankylosis.

atrophic, hard, adherent and immovable, showing many minute dilated capillaries and venules, but not showing the network of veins nor the loose baggy quality so characteristic of anetoderma. The skin of the calf was soft and pliable, not particularly thinned, but nevertheless shiny and lacking the usual markings. Sebaceous openings were not visible.

The left thigh showed changes like those on the upper extremities, but more advanced. There was atrophy of the soft parts beneath, and a band of hard skin extended from the pubic region to the internal condyle. There was an island of apparently normal skin about an inch and an eighth by eight inches on the anterior aspect of this thigh. The border was irregular. The earliest change seen in tiny isolated spots near the border and in broader areas at the

margin appeared to be a thinning of the epidermis, and perhaps of the derma also, producing a brownish violet depression. Further within the diseased area the color became more brownish and less lavender, and, especially in the lower part, the epidermis was further altered by the appearance of a fine thin translucent scaling. Over the knee, the scales became a little thicker and more

Fig. 8.—Extent of disease, atrophy of left labia and of entire left lower extremity.

opaque, and the thickness and the opacity increased in the lesions lower down on the leg until the scales were replaced by thick crusts, covering ulcers. The ulceration, indeed, seemed to be the result of a spontaneous breaking down of the skin beneath thick crusts rather than of traumatism. In one spot a loss of continuity in the epidermal covering seemed to be caused by the shrinking, laterally, of the thin atrophic skin.

The diseased area extended upward to the anterior superior spine of the ilium, and thence the upper border ran horizontally backward. The fold of skin covering Poupart's ligament was brown and atrophic, with shiny white dots in it, but below Poupart's ligament there was a triangle of nearly normal skin about an inch and a half wide at the base, extending about 3 inches

Fig 9.—Extent of disease on left side of trunk. The slight atrophy in the skin covering the upper part of the scapula does not appear in the illustration.

downward on the inner surface of the thigh. The upper border of the diseased area extended forward and downward across the mons veneris to the middle of the right Poupart's ligament, and thence downward on the inner surface of the thigh. There was no free triangle on the inner surface of the right side, but a band of approximately normal skin about an inch and a quarter wide extended downward from the right anterior superior spine nearly to the inner

aspect of the right knee. The process on the right side was very much like that on the left, but was not so extensive nor so well defined, and there was much less atrophy. Over the right knee, the skin was thin, atrophic, translucent, showing fine wrinkles when the leg was extended, but there was no superabundance of skin, and it was hard to pick it up in a fold, although there was no adhesion to bone. Just below the tubercle of the right tibia there was an area about half an inch by an inch, where the skin was more atrophic than elsewhere on the leg, beginning to adhere to the bone and developing small circular and oval pits, at the bottom of some of which was a thin dry crust. On the right calf, from knee to ankle, was a band of apparently normal skin

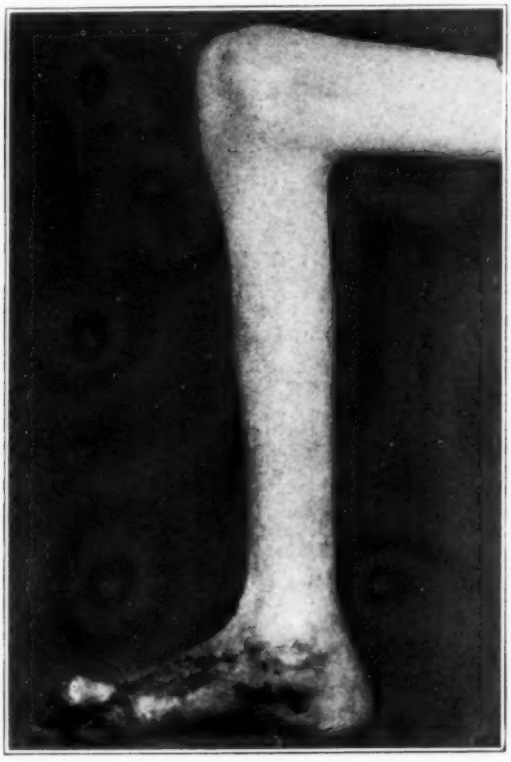

Fig. 10.—Atrophy of right leg and ulceration of foot.

about an inch wide, with a cyclic border, the diseased skin at the edge being pale lavender, thin and smooth. Adhesion of the skin to the shin was becoming quite definite about the middle of the leg. The right foot showed a shallow ulcer, partly covered with crusts, about one inch broad, over the inner half of the dorsal surface, extending on to the great toe. There was no hidebound appearance anywhere on this foot except around the ulcer. The other toes were normal.

On Jan. 16, 1923, the patient was sent to Dr. H. M. Imboden for roentgen-ray examination. He reported that there was nothing to indicate destruction of the pituitary. The clinoidal processes were well defined and seemed normal

in all respects. There were no signs of increased intercranial pressure. The teeth showed no indications of apical infection. Examination of the spine showed nothing unusual. The examination of the left leg revealed a streak of increased density projecting from about the middle to the level of the epiphyseal line, and below through to the insertion of the tendo Achillis. There

Fig. 11.—Anterior view of left leg.

was considerable atrophy of the bones, especially those of the foot. The os calcis, astragalus, cuboid and the rest of the tarsal bones were almost completely atrophied.

Dec. 20, 1922, the patient was examined by Dr. Randall Hoyt, with a view to determining the neurologic relations of the disorder. He reported as follows:

SENSIBILITY

Touch: Normal except over scarred areas, which were inconsistently anesthetic.

Heat and Cold: Normal both in perception and differentiation.

Fig. 12.—Outer aspect of left leg showing atrophy of third and fourth toes.

Pain: Hyperesthesia below the clavicles, and especially on the left side of the body anteriorly. There was a band of hyperesthesia about 2 inches wide extending along the left of the posterior midline of the body from the interscapular space to the sacrum.

Vibration: Normal.

Movement Sense: Normal (even in the involved parts).

Olfaction and Gustation: Not tested but subjectively normal.

Vision: Acuity, normal. Visual fields (finger test), normal. Optic disks, normal.

Audition: Acuity, normal and equal in both ears (air conduction of tuning-fork). Bone conduction, equal in both ears and less than air conduction (normal). Weber test normal.

Fig. 13.—Inner aspect of left leg.

MOTILITY

Atrophy and deformity (see special heading).

Motility: Muscular effort is normal, but it does not always produce movement, on account of the ankylosis.

Tonicity: Normal.

Finger-Nose Test: Normal, eyes open or closed.

Pointing Tests: Normal, eyes open or closed (no past-pointing).

Equilibration: Not tested on account of difficulty in walking.

Gait: Not tested on account of difficulty in walking.

Diadokokinesis: Normal.

Involuntary Movements: No abnormalities (tremors) observed.

Associated Movements: Apparently normal.

Deep Reflexes: Jaws, very active and equal. Pectorals, very sluggish, possibly absent.* Bicipitals, very sluggish, possibly absent.* Tricipitals, very sluggish, possibly absent.* Right patellar: active. Right Achilles: moderately active. (Left patellar and Achilles reflexes not tested on account of ulceration.)

Superficial Reflexes: Abdominals very active. (Plantar reflexes and clonus not tested on account of ulceration.)

Ocular Movements: Movements of eye and eyelids normal in all directions. Nystagmus with eyes in extreme lateral position. Pupils, medium, round, equal, react normally to direct and consensual light stimulation and to accommodation.

Facial Movements: Normal.

Masticatory Movements: Normal.

Pharyngeal Movements: Normal.

Lingual Movements: Tongue symmetrical, protrudes in the midline, but it seems difficult for the patient to hold it steady. There is no tremor in the sense of fibrillation, but there are occasional jerky movements of the whole organ. Movements from side to side are normally performed.

Cephalogyric Movements: Normal.

INVOLUNTARY MECHANISMS

Vasomotor, gastro-intestinal, urogenital systems, normal.

CEREBRATION

Organic reactions normal. (No convulsions, apraxia, aphasia, or astereognosis.)

Psychic Reactions: Patient seems unusually bright mentally, and unusually stable emotionally.

ATROPHY AND DEFORMITY

It is highly probable that the term atrophy, except as applied to the skin, is a misnomer, as the parts have failed to grow, rather than have actually shrunken.

Movement of both hip joints is normal. Movement of the right knee is normal. The left knee is immobile and is ankylosed in a flexed position. The skin over the left knee is so atrophic that one can almost see the bones beneath it. Movement of both ankles is limited. Movement of the toes is limited and is proportionate with the destruction above mentioned.

INTERPRETATION

Evidence of Involvement of the Nervous System.—1. Dissociation of the deep reflexes. The contrast between the extreme activity of the jaw reflexes and the extreme sluggishness of the reflexes of the upper extremity was striking. Even the right patellar reflex was markedly less active than the jaw reflexes.

2. Distribution of the skin lesions: The subcostal lesions on the right side correspond to the radicular distribution of the 10th dorsal segment, and on the left side to the 10th and 11th dorsal segments. The groin lesion on the right side corresponds to the 1st lumbar segment, and the groin and thigh lesion on the left side correspondes to the 1st and 2nd lumbar segments. The lesion

* Reinforced.

on the left leg corresponds to the 1st sacral segment, which lesion would permit the great toe to escape. On the right leg the 5th lumbar segment is involved, which explains the involvement of the right great toe.

3. The hyperesthesia. This is greater on the left than on the right side (that is to say, it is found on the side on which the skin lesions predominate). The band of hyperesthesia next to the posterior midline on the left side is extremely suggestive, in that this area is supplied by the posterior divisions of the spinal nerves before they have entered plexus formation.

The above findings are not only suggesitve of involvement of the nervous system, but also suggest that this involvement is limited to afferent (sensory) nerve pathways.

The older conception of "trophic centers" in the nervous system is gradually being dispelled. The arrangement of the nerve mechanism in both voluntary and involuntary nervous system are essentially the same. Each depends on three neuron reflex circuits, one neuron of which brings peripheral stimuli to the central nervous system, another of which conveys impulses from the central nervous system to a motor or secretory end-organ, and a third neuron (or system of neurons) which joins the above afferent and efferent neuron. The difference between the voluntary and involuntary lies in the fact that in the former, the cell bodies of efferent neurons lie in the ventral horns of the spinal cord, whereas in the latter they lie in the sympathetic ganglions. The connector neurons in the former instance therefore lie entirely within the central nervous system, whereas in the latter instance they pass out of the central nervous system as gray rami communicantes to the sympathetic ganglions. Neurotrophic disorders, just as motor disorders, may be caused by involvement of any one of these neurons. The Charcot joints of tabes and the trophic disturbances of syringomyelia are accompaniments of neurologic disorders in which involvement of afferent or connector systems of neurons form the pathologic characteristics.

In the present case, such neurofunctional abnormalities as are demonstrable are sensory in character, whereas the motor functions (except those abnormalities caused by ankylosis) are strikingly normal. It therefore seems logical to assume, tentatively at least, that the afferent neurons of the involuntary reflex circuits are diseased, and are responsible for the patient's condition. The fact that the skin lesions follow the radicular distribution of spinal nerves makes it seem highly probable that the actual pathologic processes lie in the dorsal root ganglions. That acute inflammation of these ganglions causes skin eruption is exemplified by herpes zoster. The generalized hyperesthesia would seem to indicate that all the dorsal ganglions (at least those on the left side) are involved, some however to a greater extent than others. Another suggestion of sensory nerve involvement is the sluggishness of the deep reflexes.

It is somewhat difficult to account for the nystagmus in this case. As it is unaccompanied by vertigo, or past-pointing, etc., it is probably not pathologic.

Treatment and Course.—Under wet dressings of red wash, the crusts were in large part softened and the suppuration greatly diminished. The ulcers on the front of the left leg healed, and there was temporary improvement in those on the left foot, but the improvement did not last, and the ulcers on the leg reappeared. The condition in May was little different from what it had been in October, except that there was less local pain and the patient was better nourished. The reappearance of ulcers over the left shin followed the development noted previously by the patient: the crusts over the scars and poorly nourished skin gradually became thicker and finally formed thick crusts under

which the devitalized tissue broke down. Various antiseptic washes and salves were used, including boric acid both in solution and in ointment, neutral acriflavine, and ichthyol, but red wash was, on the whole, the most satisfactory. Pituitary extract was given at first, but with no evident effect.

COMMENT

This case presents several unusual features. In the first place, it is not common to observe any form of scleroderma in the first few years of life, although cases have been reported at all ages from infancy on. In this case the onset occurred at about 7½ years of age, and the disease has been progressive ever since.

Not only the age but the mode of onset also is unusual, and, what is more, it is different in different places. There is no doubt that there was a distinct swelling of the left knee when the patient was first seen, and, according to the history, this was the first symptom observed. The swelling lacked the heat and tenderness of an inflammatory reaction, and reminds one of the swellings noted in the early stages of acrodermatitis chronica atrophicans. There was noted at the same time "a dermatitis extending from the ankle to the groin," and this might be interpreted as the analogue, on the lower extremity, of the typical ulnar band of acrodermatitis. But the onset on the left flank appears to have been with a change in color only, without thickening. Of course this change in color may have been preceded by a thickening which passed unnoticed, but this is not probable when we consider the development of the disease on the upper extremities. It is noteworthy that the lesions on the upper extremities were not mentioned in the first description at the Presbyterian Hospital, in the case report when presented five months after the onset of the disease, nor in the description on admission to the Presbyterian Hospital in the spring of 1922, when a careful examination was made. The patient now states that about three years ago she found it difficult to extend fully the fingers of both hands, but denies any pain or swelling.

There have never been any swellings on the upper extremities, nor is there any evidence here of adhesion of skin to bone, of hidebound skin or of baggy skin over the elbows. The course here has been entirely different from that on the legs, and yet the disease seems to be the same, for the appearance of the skin on the borders of the process on the trunk and thighs is identical with that on the forearms. The course presents another peculiarity in that the parts first affected are not those now most seriously involved. The inner aspect of the left ankle and knee, and the left flank were attacked simultaneously, but the ulceration is most severe on the outer surface of the left foot, and becomes progressively less upward. The ulceration seems to depend on distance from body center rather than on the age of the process.

In connection with the variability in the course and onset of the disease on different parts of the body should be mentioned the great diversity of lesions as now seen, ranging from barely perceptible atrophic spots, through parchment-like atrophy, to obstinate ulceration. Except in a few places, as in the left flank and the left groin and thigh, the legs, and around the ulcers, there is no thickening of the skin at all. Wherever any thickening occurs, it seems to be a late stage of the disease, not an early one. The course seems to be from a scarcely perceptible atrophy at the onset to a thin parchment-like condition, and then to a boardlike hardness with atrophy of all the subjacent parts, whether flesh or bone. One of the illustrations shows a distinct atrophy of the left labia.

The origin and extent of the ulceration are both most unusual. The gradual change from a thin translucent scale to a thick crust covering an ulcer has already been described. The occurrence of extreme ulceration in scleroderma is rare, and I know of no case approaching this one in this respect. The case most resembling it is described by Ruete and pictured on Plate 59 of Jacobi's "Ikonographia Dermatologica." The patient there shown was a boy in whom the disease had existed practically from birth, forming a sclerodermatous band extending from the anterior superior iliac spine along the posterior surface of the thigh and leg, and curving forward over the external malleolus to the dorsum of the foot. The ulcerated area formed a band about 2 cm. wide from the gluteal fold to a point about a fingerbreadth above the external malleolus, interrupted for about half an inch in the popliteal space. The knee was fixed in flexion at a right angle by the sclerodermatous tissue. The rest of the skin was normal, and examination revealed no abnormalities in the nervous system, viscera, bones or muscles.

Another somewhat unusual feature was the appearance of the right knee when the leg was extended. The skin here was brownish, thin and translucent, and thrown into many fine folds, so that it closely sesembled that seen in acrodermatitis, but although still movable, it was a little more closely attached to bone than normal, so that the first appearance of redundancy proved to be entirely fallacious.

The atrophy of the bones is a marked feature and apparently is progressive. The disintegration of the left knee joint is well advanced, while even the right shows traces of absorption of bone, as shown by comparing the roentgenogram taken at the Presbyterian Hospital in July, 1918, with that taken in January, 1923. The disintegration in the left foot is even more evident.

Along with this atrophy and ankylosis there is a progressive calcification which appears in both patellar ligaments, and to a much greater extent in the left tendo Achillis, as is shown in the roentgenograms.

Calcareous deposits in connection with scleroderma are recorded by Pollitzer,[1] but in that case they occurred in the skin lesions themselves.

As above stated, treatment has been unsatisfactory. Within the past few weeks, ionization with iodid of potassium, as recommended by Jeanselme,[2] has been tried, and although it is too soon to make any definite report, the results so far are encouraging. Jeanselme recommends a current of 10 milliamperes for half an hour, the negative pole, covered with a large pad soaked in 1 per cent. solution of iodid of potassium, being placed over the lesion, and the positive pole, wet with physiologic sodium chlorid, being placed on the skin near by. In the present case, the negative pole was placed on the dorsum of the right foot and the positive pole on the sole. We have found it impracticable to use as strong a current as 10 milliamperes, or to continue the treatment for half an hour, but have found that from 5 to 8 milliamperes for fifteen or twenty minutes was usually well tolerated, and with this dosage the ulcer has become much cleaner, with less crusting at the edges, which are not so elevated as before, and which have grown in a little over the ulcerated area. It is useless to speculate on the mode of action of this treatment until we have more assurance that it is really effective.

As in all dermatoses of obscure nature, the question of etiology is the most interesting, as it is only by the solution of this problem that we can arrive at a rational treatment. Whatever the ultimate cause may be, the only explanation of the distribution of the lesions is by action through the local blood supply or through the nervous system. In this particular instance, the lesions do not follow the distribution of any artery or group of arteries, but they do conform to the peripheral distribution of definite spinal segments, as pointed out in the report of Dr. Hoyt. Although this correspondence does not always occur, it is hard to believe that it is entirely accidental in cases like the one here reported. Steven [3] has recorded the necropsy of a woman, 26 years of age, with atrophy and scleroderma of twelve years' duration, involving the entire right side of the body, the scleroderma involving the left side to a certain extent also, in which he found definite changes in the left motor area of the brain and in the cord. Granted that scleroderma is a trophic disturbance due to lesions of the central nervous system, the inquiry is only pushed a step further back: What is the cause of this nervous disease? It may well be that any one of several toxic irritants may serve as the exciting cause, and it may be that the nervous system does

1. Pollitzer: Jour. Cutan. **36**:271 (May) 1918.

2. Jeanselme, Bourguignon and Lucas: Bull. Soc. franç. de dermat. et syph. **29**:247, 1922.

3. Steven: Glasgow M. J. **50**:401, 1898.

not function properly on account of the lack of some endocrine incretion, which would be one way of explaining the cases of scleroderma which are undoubtedly benefited by treatment with thyroid or with pituitary substance.

114 East Fifty-Fourth Street.

DISCUSSION

Dr. Harry G. Irvine, Minneapolis: I think this is an interesting case, but taking into consideration the history and the illustrations, I do not understand how it can be classed as an idiopathic atrophy. I believe the condition is a scleroderma. It seems to me that the ulcers are due directly to atrophic changes and the accompanying lesions of the skin. Some of you may remember the case I presented before the Dermatological Section at the meeting of the American Medical Association in Minneapolis. I saw that case again last year, and the process had continued in the body, and the patient had some ulcers on the internal malleoli. The atrophy of the skin still presented the classical symptoms, and the man had reached a feeble old age.

I have some photographs of sclerodactylia in which calcareous deposits are shown around the fingers as well as absorption of bone.

Dr. Fred Wise, New York: Having seen this patient at the Vanderbilt Clinic in 1918, I was shocked at the ravages the disease had caused in five years. I was also struck with the value of the follow-up system. The patient was seen only once at our clinic, but her condition would have been just as bad had we seen her every day.

Dr. Williams had little opportunity in the time at his disposal to go into details about this case. If he had, he would have commented on the literature. Scleroderma occurs in cases in which the bone is the first tissue involved, and this patient is a remarkable example of such a condition. Such cases have been reported by several writers, and the interpretation of the disease as a whole is one of progressive scleroderma, not atrophy. If the patient has atrophy of the skin, it is secondary to the sclerodermatous process.

Another point the patient illustrates well is a fact which has been brought out on several occasions during this meeting, and that is that various agents may bring about the same form of disease. In this disease we have almost indisputable evidence that nerve lesions bear a close resemblance to the bone lesions which this child had. On the other hand, there are many cases of scleroderma in which the neurologists cannot demonstrate any nerve lesions. They may be present, but they are not demonstrable.

Dr. Charles M. Williams, New York: Dr. Irvine called attention to the fact that the ulcers were due to nerve change and not to dermatitis. I agree with him. They are trophic ulcers occurring in scleroderma, and if scleroderma is a nerve disease I shall not quibble with him. I think the patient's lesions are distinctly nerve lesions.

Dr. Wise said the condition was scleroderma rather than atrophy of the skin. I think we are arguing about terms. The thing is still unsettled. The entire process is atrophic from start to finish in these cases, and in the legs the atrophy seems to be the essential thing, the hardness occurring later. However, I think that may occur in scleroderma. I was much interested in what Dr. Wise said about the bone changes in scleroderma. They have been noted, and cases of scurvy with changes in the bones of the face have also been noted.

THE VALUE OF THE KAHN PRECIPITATION TEST IN THE DIAGNOSIS OF PRIMARY SYPHILIS AND ITS ADAPTATION TO LOCAL FLUIDS *

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AND
LESTER C. TODD, M.D.
CHARLOTTE, N. C.

The early diagnosis of primary syphilis is universally recognized as of prime importance in the treatment and prognosis of the disease. The appearance of the lesion, the character of the discharge and the presence or absence of induration are all important clinical findings, yet they are not infallible in the establishment of a positive diagnosis. A demonstration of *Spirochaeta pallida* in the fluid from the sore has been until recently the only positive criterion at the disposal of the clinician. In many instances these organisms cannot be demonstrated, due either to the fact that the lesion has been treated or that it is complicated by chancroidal infection. In rare instances examination of the untreated, uncomplicated lesion fails to reveal the organisms even on repeated search. A positive diagnosis, therefore, of a suspicious lesion, is often fraught with many difficulties. Any method that will aid in the establishment of a definite diagnosis in such cases should be investigated both as to its reliability and its practicability.

Klauder and Kolmer,[1] in 1921, reported their results with the Wassermann test performed on the secretion, transudates and exudates in syphilis. They concluded from their work on chancre fluids that the fluid probably contained a complement-fixing antibody and that the local Wassermann test might be a possible aid in differentiating syphilitic from nonsyphilitic lesions. In a later [2] communication, they reported the results of the examination of fluid from fourteen cases, twelve of which were positive and two negative. Stern and Rypins [3] recently reported that they had obtained positive Wassermann reactions on fluids from thirty-four chancres, and a negative Wassermann reaction

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* Read at the Forty-Sixth Annual Meeting of the American Dermatological Association, Ann Arbor, Mich., June 7-9, 1923.

1. Klauder, J. V., and Kolmer, J.: The Wassermann Test with Secretion Transudates and Exudates in Syphilis, J. A. M. A. **76**:1635 (June 11) 1921.

2. Klauder, J. V., and Kolmer, J.: Wassermann Test Performed with Chancre Fluids as an Aid to the Early Diagnosis of Syphilis, Arch. Dermat. & Syph. **5**:566 (May) 1922.

3. Stern, D., and Rypins, H.: The Local Wassermann in the Early Diagnosis of Syphilis, J. Lab. & Clin. Med. **8**:86 (Nov.) 1922.

in two nonsyphilitic cases. They concluded that the Wassermann reaction is practical and a valuable means of diagnosing primary syphilis. As a further aid in diagnosing these cases, we have evolved a micromodification of the Kahn precipitation test that is equally valuable and accurate. Due to the simplicity of the test, we feel that it should occupy a place in our diagnostic armamentarium.

HISTORY

Since the successful advent of the complement-fixation test for syphilis, there have been research endeavors by numerous workers with the view of devising a diagnostic method which would be equal in significance and accuracy to the test known as the Wassermann reaction and yet at the same time would be less cumbersome and time consuming. A brief review of the subject indicates that there have been two chief schools of thought: One which believes that the Wassermann reaction is an antigen-antibody phenomenon, while the other tries to explain the reaction in terms of the physics and chemistry of colloids. The latter idea is the basis of the course of development that has led to the precipitation reactions. Beginning with the flocculation reaction of Meinicke [4] in 1917, there soon followed the later modification of Sachs-Georgi,[5] Dreyer and Ward,[6] Wang [7] and most recently in this country the method of Kahn.[8]

Numerous workers have made comparative studies of the parallelism of the Wassermann reaction and the Sachs-Georgi. Those reporting the highest percentage of complete agreement in this country are Parker and Haigh,[9] who report a 93 per cent. agreement in 520 cases, and Levin and Peterson,[10] 92 per cent. in 1,042 cases. The method devised

4. Meinicke: Ueber eine neue Methodik der serologischen Lues-diagnostik, Berl. klin. Wchnschr. **54**:613, 1917. Ueber Theorie und Methodik der serologischen Lues-diagnostik, ibid. **55**:83, 1918. Zur Methodik der serologischen Lues-diagnostik, München. med. Wchnschr. **65**:1379, 1918. Ueber die dritte Modifikation meiner Lues-reaktion, ibid., 1919, No. 33, p. 932.

5. Sachs, H., and Georgi, W.: Zur Serodiagnostik der Syphilis mittels Ausflockung durch Cholestermierte Extrakte, Med. Klin., 1918, No. 33, p. 805.

6. Dreyer, Georges, and Ward, H. K.: A Simple Quantitative Serum Reaction for the Diagnosis of Syphilis, Lancet **1**:956 (May 7) 1921.

7. Wang, C. Y.: A Precipitation Test for Syphilis, Lancet **1**:274 (Feb. 11) 1922.

8. Kahn, R. L.: A Simple Quantitative Precipitation Reaction for Syphilis, First Communication, Arch. Dermat. & Syph. **5**:57 (May) 1922. Second Communication, ibid. **5**:734 (June) 1922. Third Communication, ibid. **6**:332 (Sept.) 1922.

9. Parker, F., and Haigh, A. V. R.: Sachs-Georgi Test for Syphilis, Arch. Dermat. & Syph. **4**:67 (July) 1921.

10. Levin and Peterson: Sachs-Georgi Reaction for Syphilis, Arch. Dermat. & Syph. **3**:286 (March) 1921.

by Kahn has given an even greater agreement with the Wassermann reaction. Ide and Smith [11] report the results of this test in 2,165 serums and obtained identical results in all serums giving more than a two plus reaction. Moody [12] reports a 98 per cent. agreement in 1,500 tests using Herrold's [13] contact modification. Keim and Wile [14] were the first to report from a clinical standpoint the value of this test in the various stages of syphilis. They conclude that it has obviously great advantages over the Wassermann reaction in: (1) simplicity of procedure, (2) rapidity of reading, and (3) reduction of the sources of error through elimination of a hemolytic system. We have devised a special method adapting the Kahn test to the fluid obtained from primary sores.

COLLECTION OF MATERIAL

The sore to be examined is first cleansed thoroughly with saline solution and then dried. Suction is applied by means of an open-bored glass syringe made by grinding off the tip as described by Gill.[15] This instrument is adaptable to practically all penile lesions, and better results were obtained with it than with any other of a number of suction instruments used by us. The author advocates the use of a 2, 5 or 10 c.c. syringe, according to the size of the lesion. In our experience, we have found the 10 c.c. Luer syringe to be the most desirable regardless of the size of the lesion. Since it covers a larger area, the edge of the instrument does not come in contact with the sore, thereby avoiding excessive pain, and furthermore a larger quantity of fluid is obtained. A smaller syringe should be used when the lesion is situated in the sulcus retroglandularis. As suction is applied, small beads of fluid appear and coalesce at the base of the ulcer. This is taken up by capillarity into small opsonic pipets, and the process is repeated until a sufficient quantity of fluid is collected. At least two pipets should be filled.

TECHNIC

Preparation of Fluid.—After collection of the fluid the tip of each capillary pipet is sealed in the flame. The sealed capsules are then centrifugated at high speed to throw down the cells and débris. When the raw fluid is used, the tip of the pipet is cut off with a sharp file so as to remove all the sediment.

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11. Ide, Sobei, and Smith: Comparative Study of Kahn and Wassermann Reactions, Arch. Dermat. & Syph. **6**:770 (Dec.) 1922.

12. Moody, W. B.: Observations on the Precipitation Reaction for Syphilis, J. A. M. A. **80**:383 (Feb. 10) 1922.

13. Herrold, R. L.: A Ring or Contact Precipitation Test for Syphilis, a Modification of the Kahn Test, J. A. M. A. **79**:937 (Sept. 16) 1922.

14. Keim, H., and Wile, U.: The Kahn Precipitation Test in the Diagnosis of Syphilis, J. A. M. A. **79**:870 (Sept. 9) 1922.

15. Gill, W. D.: A Simple Aid in the Diagnosis of Syphilis from the Primary Lesion, J. A. M. A. **79**:966 (Sept. 16) 1922.

This leaves the perfectly clear fluid for the test. When an inactivated portion of the fluid is to be used, a sealed capsule after centrifugation is immersed upright in a water bath for thirty minutes at 56 C. After inactivation the capsule is cut as described above, and the clear fluid is used in the test.

Antigen.—The antigen is prepared and cholesterinized in accordance with Kahn's most recent method. It is diluted with saline in the usual proportion of 1:3, and the proportion of one part of diluted antigen to six parts of fluid is maintained.

Performance of the Micro Test.—On account of the relatively small amounts of fluid that are usually available for the test, we resorted to the use of blood diluting pipets (white cells) both for measuring the antigen and fluid and also for mixing. The contents of the open capsule are expelled on a clean microscopic slide. One part of the diluted antigen is taken up in the pipet and deposited on another clean slide. Six parts of the fluid are then taken up with the same pipet and added to the drop of antigen on the slide. The two reagents are then mixed as thoroughly as possible by drawing them up and down several times in the pipet and stirring the drop. A portion of the mixed fluid is then deposited by means of the pipet in the center of a clean cover slip, which is immediately covered with a deep culture slide previously ringed with petrolatum. The slide is then pressed down air-tight and turned over so as not to disturb the drop on the cover slip. The completed set-up is then placed in the incubator and observations made four hours, eighteen hours, thirty-six hours, and so on, later. In the positive cases there is a definite precipitate plainly visible macroscopically at the end of eighteen hours (Fig. 1). In some cases it was possible to see a heavy precipitate in four hours. Those cases which were positive to the naked eye at the end of eighteen hours usually showed a definite microscopic precipitate within a few hours after setting up the test. It is necessary to set up a serum control at the same time, and also a hanging drop of the antigen alone should be prepared to make sure that the antigen itself does not show a precipitate. There is always a small amount of precipitate seen microscopically in the antigen and also in the antigen and negative fluid mixture. This amount may be disregarded in the reading of the unknown.

DISCUSSION OF THE METHOD

It is important that the antigen and fluid be thoroughly mixed. It appears that the speed of the reaction is dependent on proper mixing. After thirty-six hours' incubation or longer, it was noted that bacterial growth, especially in inactivated specimens, gave a false precipitate. In the majority of raw specimens, bacterial growth does not occur early and consequently does not interfere. It is always possible to distinguish bacterial colonies from the lipoid precipitate by means of the low power microscope. At present we are working with the view of finding a suitable antiseptic that will entirely obviate this difficulty. The amount of fluid necessary for the test is small and depends on the individual blood counting pipet as these all vary in size of the capillary tube. With our pipets the minimum amount of fluid necessary varied from 0.013 to 0.028 c.c.

Early in the use of the Kahn test on the chancre fluid it was noted that the reacting substance was found early in the raw fluid from the

TABLE 1.—*The Clinical Diagnosis and Laboratory Findings in Fifty Cases of Penile Lesions*

	Clinical Diagnosis	Dark Field	Blood Wassermann Test		Kahn Test	Local Kahn		Local Wassermann Test	Treatment	Remarks
			37 C.	8 C.		Raw	Heated			
1	Chancre	Positive	++++	++++	++++	++++	++++		None	
2	Chancre	Negative	++++	++++	++++	++++	++++		Local	
3	Chancre	Negative	+	+	++	++++	—		Local	
4	Chancre	Positive*	++++	++++	++++	++++			Local	
5	Chancre	Positive	++++	++++	++++	++++	—		Local	
6	Chancre	Negative	+++	++++	++	++++	++++		Local	
7	Chancre	Negative	++++	++++	++++	++++	++++		Local	
8	Chancre	Positive	—	++++	++	++	—		None	Under influence of alcohol
9	Chancre	Positive	—	—	—	—	—		None	No alcohol, 7 days later
10	Chancre	Positive	—	—	—	++	—		Local	
11	Chancre	Positive*	—	—	—	++++	—		Local	
12	Chancre	Positive	—	—	—	++++	—		Local	
13	Chancre	Positive	—	—	—	++++	+		None	
14	Chancre	Positive	—	—	—	—		++++	Local	Twelve hours' duration
15	Chancre	Positive	++++	++++	++++	++++		++++	Local	
16	Chancre	Positive*	++++	++++	++++	++++		++++	None	
17	Chancre	Positive	++++	++++	++++	++++		+++	Local	
18	Chancre	Positive	—	—	—	++		++	Local	
19	Chancre	Negative	+++	+	++++	++		++++	Local	
20	Chancre	Positive	—	—	+	++++		—	Local	
21	Chancre	Positive	++	++	++++	—			Local	
22	Chancre	Negative	++++	++++	++++	++++			Local	
23	Chancre	Positive*	+	+	++	+++			Local	
24	Ulcus mixte	Positive	+	A-e ‡	—	++++			None	Induration pronounced
25	Ulcus mixte	Negative	—	—	—	—			None	Wassermann test repeatedly negative
26	Ulcus mixte †	Negative	—	—	—	—		++++	None	
27	Ulcus mixte †	Positive	++++	++++	++++	++++		++	Local	
28	Ulcus mixte	Negative	—	—	—	++++			Local	
29	Ulcus mixte	Negative	—	—	++++	++++			Local	
30	Ulcus mixte	Negative	++++	++++	++++	++++		++++	Local	
31	Ulcus mixte	Positive	++++	++++	—	++++		+++	Local	
32	Ulcus mixte	Negative	—	—	+	++++	++++		Arsph.	
33	Chancroid	Negative	—	—	—	—	—		Local	
34	Chancroid	Negative		—	—	—	—		Local	Wassermann test repeatedly negative
35	Chancroid	Negative	—	—	—	++++	—		Local	Treated syphilitic
36	Chancroid	Negative	—	A-e.	++++	—	—		Local	
37	Chancroid	Negative	—	—	—	—		—	Local	
38	Chancroid	Negative	—	—	—	—		—	Local	
39	Chancroid	Negative	—	—	—	—		—	Local	
40	Chancroid	Negative	—	—	—	—		A-e.	Local	
41	Chancroid	Negative	—	—	—	—		—	Local	
42	Chancroid	Negative	—	—	—	—		A-e.	Local	
43	Chancroid	Negative			—	—			Local	
44	Chancroid	Negative	—	—	—	—			Local	
45	Herpes progenitalis	Negative	—	—	—	—			Local	
46	Scabies	Negative	—	—	—	—		+	Local	
47	Balanitis erosiva	Negative	—	—	—	—		A-e.	Arsph.	Latent syphilitic
48	Balanitis erosiva	Negative	++++	++++	++++	++++			Local	
49	Bubo	Negative	—	—	—	—				
50	Traumatic ulcer									

* Dark field positive only after prolonged aspiration.

† Lesions subsequently proved to be chancroids. Blood Wassermann tests remained negative over a period of months.

‡ A-e = Anticomplementary.

local lesion, and its reacting properties were promptly destroyed by the heat of inactivation. It was soon found that an early positive Kahn reaction could not be obtained with the inactivated fluid from the local lesion. For this reason the raw fluid only should be used. This, of course, is contrary to the method of procedure when the blood serum is used in the precipitation test, since the blood serum specimens must be inactivated before use. We have tested numerous raw blood serums and in some have failed to obtain precipitation reactions, whereas, after inactivation, portions of these same specimens would give their characteristic reactions parallel with the clinical findings and the Wassermann reaction.

ANALYSIS OF CASES

In analyzing the fifty cases examined, we found twenty-three chancres, seven cases of ulcus mixte, fourteen chancroids, one herpes progenitalis, one scabies, one bubo, two balanitis erosiva and one traumatic ulcer.

CHANCRE

Dark-field examinations of the fluids from the twenty-three chancres showed the presence of *Spirochaeta pallida* in sixteen instances, or 69.5 per cent., while they were absent in seven instances, or 30.5 per cent. In three of these positive cases the organisms were not demonstrated until after prolonged suction had been applied. It is therefore advisable to repeat the dark-field examination after suction in the previously negative cases. Of the seven cases that were negative in the dark field, all showed a positive blood Wassermann and blood Kahn reaction. Twenty-one of the twenty-three chancres, or 91.3 per cent., were positive in the raw fluid by the micro-Kahn test. In one of the negative cases the lesion had been present only twelve hours, and possibly the reacting substance had not appeared. This was the only early lesion in our series. Others of three and four days' duration gave positive reactions. The second negative case was slightly positive in the blood Wassermann test, strongly positive in the blood Kahn test, but negative in both the local Wassermann and local Kahn test. Of the twenty-one positive cases, seventeen were four plus, two were three plus and two were two plus. The inactivated fluid was examined in eleven instances and found to be definitely positive in only four. In each of these cases the blood Wassermann test was also positive. Of the seven cases showing a negative reaction, six showed a negative blood Wassermann test and one a weakly positive test. Possibly there are at least two substances capable of giving the precipitation reaction—the one found early in the local lesion, which is thermolabile, while the other is thermostabile and appears in the blood stream later. The latter may be present in the local lesion coincident with its appearance in the blood

serum. It appears in the blood stream at about the same time as the appearance of the positive Wassermann reaction on the blood. Or it may be that the heat of inactivation is sufficient to destroy all of the reacting substance present in the local lesions early when the amount is small, but does not destroy all of that present in the local fluid later or in the blood serum when the amount present has greatly increased. The fact that heated serum has often a more powerful flocculating reaction than raw serum appears to be due to heat diminishing or destroying the antiflocculant action of the otherwise inactive globulin, as shown by Mackie [16]

Case 10 was of unusual interest in that the dark-field examination was positive and all other tests negative on the first examination. When this examination was made, the patient was under the influence of

TABLE 2.—*An Analysis of the Cases of Chancre*

	Cases	Percentage
Chancres positive in the dark-field examination	16	69.5
Chancres negative in the dark-field examination	7	30.5
Chancres with a positive blood Wassermann test	15	65.2
Chancres with a negative blood Wassermann test	8	34.8
Chancres with a positive blood Kahn test	16	69.5
Chancres with a negative blood Kahn test	7	30.5
Chancres with a positive local Kahn test	21	91.3
Chancres with a negative local Kahn test	2	8.7
Chancres with a positive local Wassermann test	6	85.7
Chancres with a negative local Wassermann test	1	14.3

alcohol. He was advised to return the following day. Due to an accident he did not return until one week later, during which time he had abstained from the use of alcohol. At this time the dark field was still positive and the fluid from the sore positive in the micro-Kahn test. The findings in this case suggest that alcohol may show the same interference on the micro-Kahn test that it is known to have on the blood Wassermann test.

ULCUS MIXTE

Nine cases were clinically diagnosed ulcus mixte. Two of these subsequently proved to be chancroids. Of the seven remaining cases, four, or 57.1 per cent., were positive in the dark field and three, or 42.9 per cent., were negative. The blood Wassermann test was positive in five, or 71.4 per cent. of the cases, while it was negative in two, or 28.6 per cent. Two of the cases showed only a one plus reaction but were placed in the positive group. Four cases, or 57.1 per cent., were positive in the blood Kahn test, while three, or 42.9 per cent., were negative. Seven, or 100 per cent., were positive in the local Kahn test. The local Wassermann test was performed in four cases, all of

16. Mackie, T. J.: The Serum Constituents Responsible for the Sachs-Georgi and Wassermann Reactions, J. Path. & Bacteriol. **26**:120 (Jan.) 1923.

which were positive. The two chancroids that were clinically diagnosed ulcus mixte were negative in the dark field, blood Wassermann, blood Kahn and local Kahn tests. In each of the cases the induration in the lesions was marked. In one case it was so pronounced that the lesion turned "en masse" when the foreskin was withdrawn. We felt confident that the latter lesion was a mixed sore, but due to the negative findings throughout, the patient was treated only locally and kept under observation. The lesion healed under local antiseptics, and the Wassermann reaction remained negative over a period of two months. Since the induration was the ground on which the clinical diagnosis was based, which subsequently proved to be incorrect, and since the patient had not used any form of local treatment, we feel that too much importance should not be attached to induration as a diagnostic finding.

TABLE 3.—*An Analysis of the Cases of Ulcus Mixte*

	Cases	Percentage
Ulcus mixte prositive in the dark-field examination	4	57.1
Ulcus mixte negative in the dark-field examination	3	42.9
Ulcus mixte with a positive blood Wassermann test	5	71.4
Ulcus mixte with a negative blood Wassermann test	2	28.6
Ulcus mixte with a positive blood Kahn test	4	57.1
Ulcus mixte with a negative blood Kahn test	3	42.9
Ulcus mixte with a positive local Kahn test	7	100.0
Ulcus mixte with a negative local Kahn test	0	.....
Ulcus mixte with a positive local Wassermann test	4	100.0
Ulcus mixte with a negative local Wassermann test	0	.....

CHANCROIDS

In analyzing the fourteen chancroidal cases, we found the dark field negative in fourteen cases and the blood Wassermann test negative in fourteen. The local Wassermann test was performed in four cases, two of which were negative and two anticomplementary. It is likely that the large amount of pus and infection in this type of case is responsible for the anticomplementary reaction of the fluid. It is a striking fact that in all of the chancre and ulcus mixte cases in which the local Wassermann test was performed, none of them showed this inhibitory reaction. The blood Kahn test was negative in twelve, one plus in one, and four plus in one case, the latter being a treated latent syphilitic case. The local Kahn test was positive in two cases, in one of which the patient had had four injections of neo-arsphenamin. This patient was kept under observation for three months, and the blood remained negative. May this lesion not have originally been a mixed sore, the spirochetes having been killed off by the neo-arsphenamin but the reacting substance in the Kahn test still being present when the test was performed? The blood in the other case remained negative over a period of two months, and the positive finding on the fluid was probably a technical error or a false positive.

MISCELLANEOUS LESIONS

The findings in one case of herpes progenitalis, one of scabies, two of balanitis erosiva, and one of traumatic ulcer, were entirely negative throughout. In the case of bubo with a latent syphilitic infection the blood Wassermann test, blood Kahn and local Kahn tests were positive; the local Wassermann test was anticomplementary.

While the micro-Kahn test is of great value in establishing a positive diagnosis, it in no way should displace the dark-field examination, but is of especial value in those cases in which the dark-field examination is negative.

SUMMARY AND CONCLUSIONS

1. The micro-Kahn test is adaptable to the early diagnosis of syphilis.

2. The test is simple, practicable and reliable.

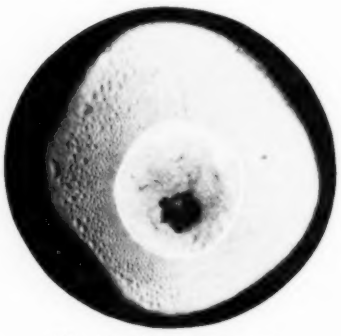

Fig. 1.—Positive Test.

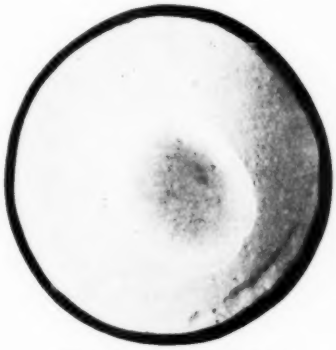

Fig. 2.—Negative Test.

3. The substance reacting in the Kahn test appears early in the local lesion and is present before the blood becomes positive in the Kahn and in the Wassermann tests.

4. The micro-Kahn test in no way should be used as a substitute for the dark-field examination, but is of especial value where the dark-field examination is negative.

5. The micro-Kahn test was positive in twenty-one of the twenty-three chancres examined, positive in seven cases of ulcus mixte, negative in ten chancroidal cases and positive in two, and negative in two case clinically diagnosed ulcus mixte which subsequently proved to be chancroids. The test was negative in one case of herpes progenitalis, one of scabies, two of balanitis erosiva, one of traumatic ulcer and positive in one of bubo in a syphilitic patient.

6. Pronounced induration in untreated cases occurs in nonsyphilitic lesions as demonstrated in Cases 26 and 27.

DISCUSSION

Dr. Louis B. Mount, Albany: I was fortunate in having the precipitation test carried out in the laboratory at Albany, and they informed me that the Kahn precipitation test is almost universally paralleling the Wassermann reaction and seems to be of much greater value than the Wassermann reaction in cases under treatment. Many of these will run along negative to the Wassermann test with the usual antigens but will still give positive Kahn reactions.

Dr. Udo J. Wile, Ann Arbor: We have had an excellent opportunity, in a small way, to compare the Kahn precipitation test with the most sensitive Wassermann tests, and the less sensitive run parallel with the Wassermann test at the Psychopathic Hospital here and at Lansing, where Dr. Kahn, I believe, has run 30,000 parallel tests. I do not believe that we should try to displace the Wassermann test, but as a complementary test this stands out. For example, in a positive serum we can get a flocculation within a few minutes that can be seen with the naked eye. I believe that the application which Dr. Elliott has made opens up an interesting new field of endeavor. We all of us see doubtful sores, and I am particularly struck with those Dr. Elliott mentioned as being indurated. We see the septic, mixed sores in which by reason of infection we do not find *Spirochaeta pallida*, and I am sure many of these patients are treated for syphilis. Some may not have it, but obviously many do. In doubtful sores the mere presence of induration in the sore which is suspicious of syphilis is not as weighty evidence as we have been accustomed to regard it. I believe this microscopic Kahn test is a valuable aid in our suspicious cases.

Dr. J. V. Klauder, Philadelphia: I was particularly interested in Dr. Elliott's contribution in view of the work of Dr. Kolmer and myself on the local Wassermann reaction of chancre fluid as a means to an early diagnosis of syphilis. I think these tests are useful. They possess specificity regardless of the presence or absence of the *Spirochaeta pallida* in the dark-field examination and regardless of whether blood is present or not in the fluid examined. Indeed, one may perhaps be justified in using it to the exclusion of a blood serum test. Dr. Elliott's method is undoubtedly more simple and practical than the local Wassermann reaction and may take the place of the local Wassermann reaction provided further observation shows that it does not give too many false positives.

Dr. E. Wood Ruggles, Rochester, New York: During the past two weeks I have had two cases of chancroid which are the first I have seen for at least two years. One thing I wish to mention is that the syphilitic chancre bleeds profusely, whereas herpes and chancroid bleed little. A great deal of suction is necessary to get any blood in these cases, and I think this is a good point in differential diagnosis. One rarely or never finds *Spirochaeta pallida* when, after curetting and drying the lesion, it is difficult to obtain enough serum for a dark-field specimen.

Dr. C. Morton Smith, Boston: I was interested in the report of the treated cases. Recently we have seen several chancres that had been treated with mercury, thereby making the dark-field examination useless. This test seems to supplement the dark-field examination and may be exactly what we need.

Dr. R. L. Kahn, Lansing, Michigan: Before saying a word about our precipitation test, I wish to say that I was glad to hear Dr. Elliott's paper and to learn that he has opened up what appears to be a new field of endeavor in

trying to determine the precipitation results with fluid from the chancre and other syphilitic lesions.

Regarding the precipitation test, having become interested in a simple test for syphilis we naturally have continued to study the many problems connected with it. One of the main problems was to overcome the necessity for prolonged incubation. After mixing serum with antigen we saw no reason why in many cases one should be required to wait from eighteen to twenty-four hours before formation of a precipitate. We believed that there must be present in this test some element which tends to delay the formation of a precipitate. We have been able finally to overcome this delaying element. By properly mixing our antigen with salt solution, a mixture is obtained which when added to proper amounts of inactivated serum gives immediate precipitation in about 95 per cent. of syphilitic serums, and the final reading is taken at the end of about one hour's incubation.

Three tubes are employed in this test with equal amounts of serum and varying amounts of antigen. Four typical reactions are obtained: complete precipitation in all tubes, complete precipitation in the tube containing the larger amount of antigen and weak precipitation in the remaining tubes, complete precipitation in the tube containing the smallest amount of antigen and weak precipitation in the remaining tubes, and no precipitation in any of the three tubes.

The limited time at my disposal does not permit me to go into detail with this reaction, but those who are interested in this test I hope will continue their interest. I believe that the precipitation test holds considerable promise for a correct serum diagnosis of syphilis. I would like to say also that if any one wishes to communicate with me regarding this test, I shall be glad to help in any way I can.

Dr. Joseph A. Elliott, Charlotte, N. C.: I wish to emphasize further the fact that the microscopic Kahn test has its greatest value as an aid in diagnosing questionable penile lesions. We all see lesions that are clinically mixed sores and yet in many instances we are unable to demonstrate *Spirochaeta pallida*. Many of these cases are seen too early for the blood Wassermann test to be of any value. A positive diagnosis can usually be made in such cases by means of the test we have devised.

COMPARATIVE SPIROCHETICIDAL ACTIVITY OF SALTS OF METALS NOT HERETOFORE STUDIED IN THE TREATMENT OF EXPERIMENTAL RABBIT SYPHILIS *

JOSEPH V. KLAUDER, M.D.

PHILADELPHIA

It is a significant fact that the known spirocheticidal drugs—arsenic, antimony, vanadium and bismuth—are in the same group (V) of the periodic arrangement of the elements. Indeed, with the exception of mercury, all the known spirocheticidal drugs [1] are in this group. Although this fact suggested for a long time possible spirocheticidal action of other metals in the same group, and the only remaining common one was bismuth, it was not until 1916 that Sauton and Robert [2] demonstrated spirocheticidal activity of bismuth in *Spirochaeta gallinarum infection in chickens,* and Sazerac and Levaditi [3] in 1921, spirocheticidal activity in experimental syphilis.

In this study the salts of other metals, particularly heavy metals, were studied for spirocheticidal action in experimental syphilis in rabbits. The following salts of these metals were employed: gold chlorid, thorium chlorid, platinum chlorid, barium chlorid, cadmium iodid, cerium nitrate, strontium nitrate, calcium chlorid, tin chlorid, zinc sulphate, uranium acetate, sodium tungstate and germanium oxid.

The known spirocheticidal metals—arsenic (arsphenamin), bismuth, antimony and vanadium were studied for their therapeutic index (the ratio between the therapeutic active dose and the maximum tolerated dose) in experimental syphilis. The following salts of these metals were employed — bismuth trioxid, sodium and potassium tartrobismuthate, potassium tartrobismuthate, potassium antimonyl tartrate, antimony tartrate, vanadium chlorid and vanadium oxid.

The remaining metals in Group V of the periodic arrangement of the elements—columbium praseodymium, ytterbium, and tantalum—were

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* Read as part of the paper "Studies in Experimental Syphilis" at the Forty-Sixth Annual Meeting of the American Dermatological Association, Ann Arbor, Mich., June 7-9, 1923.

* From the Research Institute of Cutaneous Medicine, Philadelphia.

1. A possible exception to this statement is margosic acid and its salts. According to Chatterji (Margosic Acid and Its Salts in Syphilis and Skin Diseases, Indian J. M. Res., April, 1918) this drug is spirocheticidal.

2. Robert, A. E., and Sauton, B.: Action du bismuth sur la spirillose des poules, Ann. de l'Inst. Pasteur. **30**:261-271, 1916.

3. Sazerac, R., and Levaditi, C.: Comp. rend. Acad. d. sc. **172**:1391, 1920; **173**:338-340, 1921.

not studied for spirocheticidal activity, since they were not obtainable at the time this study was conducted. Moreover, these metals are rare, and a demonstration of spirocheticidal activity would be more of scientific interest than of practical importance.

STANDARD ADOPTED IN STUDYING SPIROCHETICIDAL ACTION OF THE METALS EMPLOYED

The results following the administration of the therapeutic active dose of arsphenamin, that is, 0.006 gm.[4] per kilogram of body weight injected intravenously in rabbits with active syphilitic testicular lesions, were taken as a standard in studying spirocheticidal action of the aforementioned metals and in determining the therapeutic active dose of the known spirocheticidal metals. These results are as follows: Before treatment, dark-field examination of the surface of the chancre or in its absence of serum obtained from puncturing testicular nodes showed many motile spirochetes in each microscopic field. Twenty-four hours after treatment, dark-field examination showed only a few slightly motile or nonmotile spirochetes and many agglutinated organisms in each field. Dark-field examinations on subsequent days were negative. Grossly, the chancre or the nodes were appreciably smaller the following twenty-four hours and gradually lessened in size until complete involution occurred within eight days. No recurrence of testicular or scrotal syphilitic lesions occurred during the following two months.[5]

METHOD EMPLOYED

Rabbits with well developed scrotal chancres or with well developed testicular nodes, the serum from which disclosed many motile spirochetes in the dark-field microscope, were injected intramuscularly with 0.1 gm. or 0.125 gm. per kilogram of body weight of one of the following: zinc sulphate, calcium chlorid, tin chlorid, strontium chlorid, cerium nitrate, cadmium iodid, sodium tungstate, uranium acetate, gold chlorid, barium chlorid, platinum chlorid and thorium chlorid. Germanium oxid was administered intravenously.

Subsequent to treatment with the foregoing drugs, the syphilitic lesion in the animal injected was observed for gross changes, and dark-field examinations were frequently conducted. This observation extended over a period ranging from ten to sixty days.

RESULTS

The results of treatment with the aforementioned drugs are shown in Table 1. It will be noted that with the exception of gold chlorid

4. The curative dose of arsphenamin is about 0.012 gm. per kilogram injected intravenously.

5. In some animals active syphilitic lesions recur after this period.

and thorium chlorid the results were frankly negative; that is, with the amount of drugs employed there was no evidence of spirocheticidal action; the syphilitic lesion remained unchanged, and no evidence of such action was apparent in the dark-field examination.

TABLE 1.—*Results of Study of Spirocheticidal Activity in Experimental Syphilis of a Number of Metals*

Drug	Grams per Kilogram	Method of Injection	Syphiloma Rabbit's Testicle	Dark-field Examination	Period of Observation
Zinc sulphate	0.100	Intramuscular	Unchanged	No effect	14 days
Calcium chlorid	0.100	Intramuscular	Unchanged	No effect	14 days
Tin chlorid	0.100	Intramuscular	Unchanged	No effect	10 days
Strontium nitrate	0.125	Intramuscular	Unchanged	No effect	8 days
Cerium nitrate	0.125	Intramuscular	Unchanged	No effect	25 days
Cadmium iodid	0.125	Intramuscular	Unchanged	No effect	11 days
Sodium tungstate	0.100	Intramuscular	Unchanged	No effect	10 days
Uranium acetate	0.100	Intramuscular	Unchanged (4 days)	No effect (4 days)	Died 5 days after treatment
Barium chlorid	0.125*	Intramuscular	Unchanged (3 days)	No effect (3 days)	Died 3 days after treatment
Platinum chlorid	0.125†	Intramuscular	Unchanged (4 days)	No effect (4 days)	Died 4 days after treatment
Germanium oxid	0.005	Intravenous	Unchanged	No effect	12 days
Germanium oxid	0.025‡	Intravenous	Unchanged	No effect	12 days
Thorium chlorid	0.100	Intramuscular	Improved	Negative 6 days; recurred; positive 15 days	15 days
Thorium chlorid	0.125	Intramuscular	Markedly improved 10 days; involuted 17 days	Negative 6 days	30 days
Thorium chlorid	0.150	Intramuscular	Involuted 9 days	Negative 2 days	Died 10 days after treatment
Thorium chlorid	0.150	Intramuscular	Marked improvement 2 days; involuted 14 days	Negative 2 days	30 days, no recurrence
Gold chlorid	0.100	Intramuscular	No change 5 days; involuted 16 days	Nonmotile spirochetes 24 hours; negative 6 days	60 days
Gold chlorid	0.150	Intramuscular	Involuted 12 days	Negative 3 days	30 days
Gold chlorid	0.200	Intramuscular	Little change 4 days	Motile spirochetes 24 hours; nonmotile spirochetes 48 hours	Died 5 days after treatment

* Normal rabbits were injected intramuscularly with 0.075 and 0.05 gm. per kilogram; death occurred in a few days.

† A normal rabbit was injected intramuscularly with 0.05 gm. per kilogram; death occurred in seven days.

‡ An intravenous injection of 0.05 gm. per kilogram killed the rabbit soon after administration.

As shown in Table 1, the amount of uranium acetate[6] (0.1 gm. per kilogram), of barium chlorid and of platinum chlorid (0.125 gm.

6. It will be recalled that uranium acetate has been employed in the study of experimental nephritis.

per kilogram of each)[7] employed killed the animal in a few days. Up to the time of death, no spirocheticidal action of these drugs was noted.

Intravenous injections of 0.005 and 0.025 gm. per kilogram of germanium oxid were negative for spirocheticidal action. An intravenous injection of 0.05 gm. per kilogram killed the animal soon after its administration.

STUDY OF THE SPIROCHETICIDAL ACTIVITY OF GOLD AND THORIUM

It is interesting to note that gold is in the eleventh series of Group I of the periodic arrangement of the elements, mercury is in the same series of Group II and bismuth in the same series of Group V. Thorium is in the twelfth series of Group IV and has an atomic weight of 232. In view of the foregoing, which possibly evidences some chemical relationship of these metals, two of which, mercury and bismuth, are spirocheticidal, it was expected that gold and possibly thorium would possess spirocheticidal properties.

Gold was employed as gold chlorid, which was administered intramuscularly in amounts of 0.1, 0.15 and 0.2 gm. per kilogram. Following treatment with 0.1 gm. there was no gross change in the syphiloma for about five days, and complete involution occurred in sixteen days. The dark-field examination twenty-four hours after treatment disclosed many nonmotile organisms (before treatment many very motile organisms were present), and an absence of organisms was not noted until the sixth day. Since this result is within the limit of the rate of disappearance of the syphiloma and of spirochetes in untreated animals, this amount of gold chlorid cannot be regarded as exerting spirocheticidal action.

Following treatment with 0.15 gm. of gold chlorid, the syphiloma involuted in twelve days; the dark-field examination was negative in three days. This amount, therefore, furnished evidence of some spirocheticidal activity. Treatment with 0.2 gm. killed the animal in five days. Up to this time, there was little evidence of spirocheticidal activity of the drug.

As shown in Table 1, there was evidence of some spirocheticidal activity of thorium chlorid. Treatment with 0.1 gm. per kilogram produced a partial involution of the syphiloma during the following ten days; the dark-field examination became negative the sixth day after treatment, but recurred positive in fifteen days, at which time the

7. Normal rabbits were injected intramuscularly with 0.075 gm. and 0.05 gm. per kilogram of barium chlorid; death occurred in a few days. Following an injection of 0.05 gm. per kilogram platinum chlorid in a normal rabbit, death occurred in seven days.

syphiloma was well pronounced. Treatment with 0.125 gm. produced a marked improvement of the syphiloma in ten days and involution in seventeen days; the dark-field examination became negative in six days. There was no recurrence; the period of observation was sixty days. Two animals were treated with 0.15 gm. of thorium chlorid; in one there occurred an involution of the syphiloma in nine days; the dark-field examination became negative in two days. In the other there was a marked improvement of the syphiloma two days following treatment; but complete involution did not occur until after two weeks, while the dark-field examination became negative in six days. One animal died ten days after treatment, while there was no recurrence in the other animal during a thirty day period of observation.

The maximum tolerated dose of thorium chlorid injected intramuscularly is about 0.15 gm. per kilogram. An intravenous injection in a normal rabbit of 0.01 gm. per kilogram of the drug killed the animal immediately after its administration. The maximum tolerated dose of the drug in white rats injected intravenously was 0.02 gm. per kilogram. This amount was not trypanocidal in *Trypanosome equiperdum* infection in white rats.

It is apparent from the foregoing that gold and thorium in the maximum tolerated dose did not exert a spirocheticidal action conforming with the standard adopted, that is, such action was not conformable to the action of 0.006 gm. per kilogram of arsphenamin. Nevertheless, there was evidence of spirocheticidal activity. Indeed, the absence of any spirocheticidal activity on the part of these metals apparently does not constitute valid reasons against the assumption that in combination with the arsenicals, particularly arsphenamin, they would not enhance the spirocheticidal properties of the latter. In this regard the spirocheticidal action of antimony is enhanced when employed in combination with an organic arsenical.

SPIROCHETICIDAL ACTIVITY OF BISMUTH, OF ARSPHENAMIN AND OF MERCURY

Intravenous injection of an aqueous solution of sodium and potassium tartrobismuthate and of potassium tartrobismuthate was very toxic; the majority of rabbits injected intravenously with more than 0.005 gm. of either of these drugs per kilogram of body weight did not survive.

It was determined that the therapeutic active dose of sodium and potassium tartrobismuthate in aqueous solution and in olive oil, and potassium tartrobismuthate in aqueous solution, was at least 0.05 gm. per kilogram of body weight and at least 0.15 gm. per kilogram of

bismuth trioxid. When this amount of the respective drugs was injected intramuscularly, the results conformed in a general way to the aforementioned standard, except that twenty-four hours after the injection more motile spirochetes were seen in the dark-field than are present twenty-four hours after an intravenous injection of 0.006 gm. of arsphenamin. However, dark-field examinations conducted on subsequent days were negative and the syphilitic lesion involuted within the specified time. This can doubtless be explained by the different method employed in administering the bismuth preparations.

The maximum tolerated and lethal doses of the bismuth preparations were determined by injecting intramuscularly normal rabbits with

TABLE 2.—*Showing Comparative Spirocheticidal Activity of Arsphenamin, Mercury, Bismuth, Antimony and Vanadium in Experimental Syphilis*

Drug	Method of Injection	Therapeutic Active Dose, Gm. per Kilogram	Maximum Tolerated Dose, Gm.	Therapeutic Index
Mercuric chlorid*	Intravenous	0.003	0.001	One-third
Arsphenamin	Intravenous	0.006	0.100	Seventeen
Sodium and potassium tartrobismuthate (aqueous solution	Intramuscular	0.050	0.125	Two and one-half
Sodium and potassium tartrobismuthate (oil suspension)	Intramuscular	0.050	0.2	Four
Potassium tartrobismuthate	Intramuscular	0.050	0.250	Five
Bismuth trioxid (oil suspension)	Intramuscular	0.150	0.400	Two and two-thirds
Potassium antimonyl tartrate	Intravenous	.....	0.010†	Less than one
Antimony tartrate	Intravenous	.....	0.015†	Less than one
Antimony tartrate	Intramuscular	0.050	0.050	One
Sodium tetravanadate, sodium hexavanadate, vandyl sulphate §	Intravenous	0.014	.....	.....
Vanadic oxid, vanadic chlorid ¶	.....	.....	.....	.....

* These figures are quoted from H. J. Nichols

† With these amounts there was little evidence of spirocheticidal activity.

§ These figures are quoted from Proescher and Seil, who studied these salts of vanadium, employing them in amounts the equivalent of 0.014 gm. of V 205 (vanadic oxid) which was two thirds of the fatal dose.

¶ These were the only salts of vanadium available; they were too toxic for spirocheticidal study.

increasing amounts of the respective drugs. The maximum tolerated dose [8] of sodium and potassium tartrobismuthate in aqueous solution was 0.125 gm. per kilogram. The majority of animals injected with 0.15 gm. and larger amounts per kilogram died. With the oil suspension of the drug, animals survived doses up to 0.2 gm. per kilogram but succumbed to injections of 0.25 gm. Animals injected with potas-

8. The majority of rabbits after receiving the maximum tolerated dose of the bismuth preparations lost in weight from 300 to 400 gm. for about two weeks following the injection. After this time, the weight gradually increased to about the weight before treatment.

sium tartrobismuthate survived doses up to 0.25 gm. per kilogram,[9] but died following injections of 0.3 gm. The maximum tolerated dose of bismuth trioxid in olive oil was 0.4 gm. per kilogram. Animals injected with 0.45 gm. and larger amounts per kilogram died.

The maximum tolerated dose of potassium tartrobismuthate was about five times the therapeutic active dose; with an oil suspension of sodium and potassium tartrobismuthate, it was four times the therapeutic active dose; with an aqueous solution of the same drug it was two and one-half times the therapeutic dose, and with bismuth trioxid in olive oil it was two and two-thirds times the therapeutic active dose.

Since the recorded therapeutic active and maximum tolerated doses of mercury and of arsphenamin are based on the intravenous administration of these drugs, their spirocheticidal action cannot be compared accurately with that of bismuth. According to Nichols,[10] the maximum tolerated dose of mercuric chlorid when injected intravenously in rabbits is 0.001 gm. per kilogram. The therapeutic active dose of arsphenamin injected intravenously in syphilitic rabbits is about 0.006 per kilogram; the maximum tolerated dose is about 0.1 per kilogram.

The aforementioned therapeutic active and maximum tolerated doses of sodium and potassium tartrobismuthate in aqueous solution and in oil suspension are about the same as reported by Sazerac and Levaditi.[11] The therapeutic active and maximum tolerated doses of the other two bismuth preparations studied have not to my knowledge been studied and reported by others.[12]

SPIROCHETICIDAL ACTIVITY OF ANTIMONY

The trypanocidal and spirocheticidal activity of antimony has long been known. Antimony in the form of potassium antimonyl tartrate (tartar emetic) has long been employed in the treatment of certain protozoan diseases in human beings and luargol, a combination product of arsphenamin base, silver bromid and antimonyl sulphate, is employed in the treatment of human syphilis.

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9. There was one exception to this: One animal died after an injection of 0.15 gm. per kilogram. All other animals injected survived this dose, and none of the animals injected with doses of 0.2 and 0.25 gm. died.

10. Nichols, H. J.: Further Observations on Certain Features of Experimental Syphilis and Yaws in the Rabbit, J. Exper. Med. **14**:202, 1911.

11. Sazerac, R., and Levaditi, C.: Etude de l'action therapeutique du bismuth sur la syphilis, Ann. de l'Inst. Pasteur. **36**:1-13, 1922.

12. A study of bismuth in the treatment of human syphilis is separately reported by Klauder, J. V.: Bismuth in the Treatment of Syphilis; Report of Clinical and Experimental Studies, Arch. Dermat. & Syph. **7**:721-744 (June) 1923.

The spirocheticidal activity of antimony in experimental syphilis has been studied notably by Dubois,[13] Uhlenhuth, Mulzer and Hugel,[14] and by Hugel.[15] In these studies, it was shown that antimony possesses some spirocheticidal activity. Hugel observed that such action is enhanced when the drug is in combination with various organic arsenicals.

Broden and Rodhain [16] employed potassium antimonyl tartrate in the treatment of human syphilis and Hugel reports on the use of some organic preparations of antimony. In these circumstances, the antimony preparations employed did not exert an energetic action.

In this study, it was observed that the maximum tolerated dose of potassium antimonyl tartrate administered intravenously was 0.01 gm. per kilogram. After treatment with this amount, there was little change in the syphiloma. The dark-field examination, twenty-four hours after treatment, showed only nonmotile organisms. There was an absence of organisms on subsequent daily examinations until the sixth day, at which time motile organisms were present. This result is almost similar to that reported by Hugel.[15] In his study, 0.01 gm. per kilogram of potassium antimonyl tartrate was administered intravenously in syphilitic rabbits. The dark-field examination in twenty-four hours showed nonmotile organisms; in forty-eight, the examination was negative, but again positive on the third day.

Antimony tartrate was also studied. It was noted that this drug is slightly less toxic than postassium antimonyl tartrate; the maximum tolerated dose in rabbits was 0.015 gm. per kilogram injected intravenously. This amount, however, did not exert any greater spirocheticidal action than 0.01 gm. of potassium antimonyl tartrate. An intramuscular injection of 0.05 gm. per kilogram of antimony tartrate exerted a spirocheticidal action comparable to that of 0.006 gm. per kilogram of arsphenamin injected intravenously. After this treatment, the animal lost about 300 gm. in weight and died forty-four days later.

In Kolmer's [17] study of the trypanocidal activity of potassium antimonyl tartrate in *Trypanosome equiperdum* infection in white rats,

13. Dubois, Paul: Etinge Versuche über die Wirkung der Antimonsalze auf die Kaninchensyphilis, Ztschr. f. Chemotherapie, Orig. I, 203-223, 1912.

14. Uhlenhuth, P.; Mulzer, P., and Hugel, G.: Die chemotherapeutische Wirkung von organischen Antimonpräparaten bei Spirochaeten und Trypanosomenkrankheiten, Deutsch. med. Wchnschr. **39**:393-394, 1913.

15. Hugel, G.: Experimentelle Beitrage zur Chemotherapeutische Wirkung von organische Antimonpräparaten bei Spirochaeten und Trypanosomenerkrankungen, Arch. f. Dermat. u. Syph. **118**:1-60, 1913.

16. Broden, A., and Rodhain, J.: Action de l'antimoine dans le pian et dans la syphilis, Arch. f. Schiffs. u Tropen Hyg. **12**:504-505, 1918.

17. Kolmer, J. A.: Personal communication.

it was observed that the maximum tolerated dose 0.02 per kilogram administered intravenously exerted a trypanocidal action comparable to 0.004 gm. per kilogram of arsphenamin.

SPIROCHETICIDAL ACTIVITY OF VANADIUM

Spirocheticidal activity of vanadium has been demonstrated by Proescher and Seil [18] who studied its action in experimental syphilis in rabbits. The vanadium salts employed were sodium tetravanadate, sodium hexavanadate and vandyl sulphate, all injected intravenously. The amounts injected were two thirds of the fatal dose. An injection of these salts of vanadium in the amount equivalent to 0.014 gm. of vanadic oxid ($V_2 O_5$), caused spirochetes to disappear from the syphiloma of a rabbit's testicle in two days, and produced complete involution of the syphiloma in eight days.

Proescher and Seil also report favorable results with vanadium in the treatment of human syphilis. The least toxic salt of vanadium employed was sodium hexavanadate, which was injected intramuscularly as well as intravenously. The amount injected intramuscularly was as high as the equivalent of 0.08 gm. of vanadic oxid and as high as the equivalent of 0.04 gm. of vanadic oxid for intravenous administration. After a single injection spirochetes disappeared from the syphilitic lesion in from twenty-four to forty hours. Treatment was administered every three days. Syphilitic lesions involuted after a total administration ranging in different patients from the equivalent of 0.07 gm. to 0.635 gm. of vanadic oxid in a period of time ranging from a few days to three weeks.

The foregoing observations of Proescher and Seil led to the inclusion of vanadium in this study. Unfortunately, the salts of vanadium they employed were not available. The only available salts were vanadic oxid and vanadium chlorid. The injection of these in rabbits was so toxic that it was not possible to study spirocheticidal activity. An intravenous injection of 0.01 gm. per kilogram of vanadium chlorid promptly killed the animal, as did likewise an intravenous injection of 0.004 gm. per kilogram of vanadic oxid. An intramuscular injection of 0.006 gm. per kilogram of the latter drug caused paralysis of the extensor muscles of the right fore leg and subsequent death of the animal.

SUMMARY

The known spirocheticidal drugs—arsenic, antimony, vanadium and bismuth—are in the same group (V) of the periodic arrangement of the elements. With the exception of mercury, all the known spirocheticidal drugs are in this group.

18. Proescher, F., and Seil, H. A.: A Contribution to the Action of Vanadium with Particular Reference to Syphilis, Am. J. Syphilis **1**:347-405, 1917.

In this study the salts of other metals, particularly heavy metals, were studied for spirocheticidal action in experimental syphilis in rabbits. The following salts of these metals were employed—gold chlorid, thorium chlorid, platinum chlorid, barium chlorid, cadmium iodid, cerium nitrate, strontium nitrate, calcium chlorid, tin chlorid, zinc sulphate, uranium acetate, sodium tungstate and germanium oxid.

The known spirocheticidal metals—arsenic (arsphenamin), bismuth, antimony and vanadium were studied for their therapeutic index (the ratio between the therapeutic active dose and the maximum tolerated dose) in experimental syphilis. The following salts of these metals were employed: bismuth trioxid, sodium and potassium tartrobismuthate, potassium tartrobismuthate, potassium antimonyl tartrate (tartar emetic), antimony tartrate, vanadium chlorid and vanadic oxid.

The results following treatment with the therapeutic active dose of arsphenamin, that is, 0.006 gm. per kilogram of body weight injected intravenously in rabbits with active syphilitic testicular lesions were taken as a standard in studying spirocheticidal action of the aforementioned metals and in determining the therapeutic active dose of the known spirocheticidal metals. These results are as follows: Twenty-four hours after treatment, the dark-field examination shows a considerable reduction in the number of organisms, many of which are nonmotile; subsequent examinations are frankly negative. There is an appreciable gross improvement of the syphiloma twenty-four hours after treatment and complete involution within eight days.

Rabbits with well developed scrotal chancres or well developed testicular nodes were injected intramuscularly with 0.1 gm. or 0.125 gm. per kilogram of body weight of one or the other of the aforementioned salts of the metals studied for spirocheticidal activity. The result of this study was entirely negative, with the exception of gold chlorid and thorium chlorid.

The result of treatment with gold chlorid and thorium chlorid in amounts of 0.1 and 0.15 gm. per kilogram (the latter amount was about the maxium tolerated dose of these drugs) showed some spirocheticidal action; such action, however, was not comparable to the action of 0.006 gm. per kilogram of arsphenamin injected intravenously.

Thorium chlorid was not trypanocidal to *Trypanosome equiperdum* in white rats.

It was determined that the therapeutic active dose of sodium and potassium tartrobismuthate in aqueous solution and in olive oil and potassium tartrobismuthate in aqueous solution was at least 0.05 gm. per kilogram and at least 0.15 gm. per kilogram of bismuth trioxid. When this amount of the respective drugs was injected intramuscularly the results obtained conformed in a general way to the aforementioned standard.

The therapeutic index of mercuric chlorid is one-third; arsphenamin, seventeen; potassium tartrobismuthate, five; sodium and potassium tartrobismuthate, in aqueous solution, two and one-half; in oil suspension, four; bismuth trioxid, two and two-thirds.

Reference is made to the recorded data regarding the trypanocidal and spirocheticidal activity of antimony. In this study, it was observed that the maximum tolerated dose of potassium antimonyl tartrate injected intravenously in rabbits was 0.01 gm. per kilogram and that this amount was only slightly spirocheticidal. The therapeutic index is therefore less than one. Antimony tartrate is less toxic than potassium antimonyl tartrate and possesses about the same spirocheticidal properties.

The work of Proescher and Seil on the spirocheticidal activity of sodium tetravanadate, sodium hexavanadate and vandyl sulphate is reviewed.

Vanadium chlorid and vanadic oxid were the only available salts of vanadium. It was observed that these salts were too toxic to study their spirocheticidal activity in experimental syphilis.

DISCUSSION

Dr. J. Frank Schamberg, Philadelphia: I have had an opportunity to keep in touch with the work which Dr. Klauder has just described, and I doubt that any one present can appreciate the immense amount of work it has required to determine whether the spirochete would be made resistant.

Dr. Klauder gave a rabbit experimentally infected with syphilis a subcurative dose of arsphenamin. After a specified period, the resulting testicular syphiloma was removed, emulsified and injected into other rabbits. The second rabbit received a larger dose: the syphiloma from this animal was removed and again injected into other animals. A still larger dose was administered, and the series thus continued. By this procedure Dr. Klauder demonstrated that ultimately a larger dose of arsphenamin would be required to cure than in control rabbits. This required investigation extending over many months. I think Dr. Klauder has established the fact that the spirochete may be rendered relatively resistant. This work has an important practical bearing: the use of very small ascending doses may tend to desensitize the spirochete to the arsenical.

With regard to the second part of the communication, this also represented an extensive piece of research work which is of importance to those interested in the chemotherapy of the disease.

Within recent years, through the activity of French investigators, another drug—bismuth—has been brought to the attention of the medical profession as a remedy in the treatment of syphilis. From the results reported thus far, it would appear that the effects of bismuth are quite comparable with those of mercury. We had in the past been accustomed to regard bismuth as an inert substance, and roentgenologists were in the habit of giving large doses to patients by mouth or by rectum to facilitate radiographic examinations. The reason these patients were not poisoned was because the drug was not absorbed. Given intravenously, bismuth is moderately toxic and may produce severe

symptoms. The chief method of administration is by intramuscular injection, and there will no doubt be a flood of new bismuth preparations brought to the attention of the profession within the next few years. There is still an opportunity for developing new drugs having a spirocheticidal action. In the early part of the last century a book was written on the treatment of syphilis with gold, in which good results were acclaimed. We have in our laboratories used a gold arsphenamin, a copper arsphenamin and many metallic arsphenamins, but the relationship of their toxicity to their therapeutic action has indicated that they are inferior to the arsphenamins ordinarily in use. Any work which tends to establish leads for the selection of new compounds capable of further chemical manipulation cannot fail to be of value. Where one investigator leaves off, another takes up the work, and the result is often of benefit.

Dr. Joseph V. Klauder, Philadelphia: The syphilitic rabbits manifesting some increased resistance to arsphenamin did not offer any increased resistance to bismuth. I think the data which I have presented, if used in a practical way, will lead us to avoid small and increasing doses of arsphenamin in the treatment of human syphilis and to employ an alternating plan of treatment; that is, a course of arsphenamin alternating with a course of bismuth and a course of mercury.

TREATMENT OF EARLY SYPHILIS*

H. G. IRVINE, M.D.

MINNEAPOLIS

During the last two decades great progress has been made in syphilology, and nearly every advance has been one which greatly improves the opportunity to deal successfully with early syphilis. The discovery of the spirochete has made it possible to identify positively the initial lesion; the Wassermann test has assisted in judging the time of the general dissemination of the disease, and arsphenamin has given us a powerful agent to render the disease noninfectious quickly, if not to cure it completely.

For several years after the achievements mentioned, efforts were devoted toward establishing a standard of treatment, and every year brought changes either in technic or in methods. During the last three or four years, however, there has been fairly general agreement on methods of treatment. It is the purpose of this paper to call attention to new drugs and methods and to attempt to outline the generally accepted methods of treating early syphilis. The term "early syphilis" is rather a general one, and may be interpreted differently by different people; in this paper, it will include the case from time of exposure until and including the first general eruption.

While the title does not include prophylaxis, the possible value of suggested methods should not be forgotten. Thorough soap and water washing followed by application of calomel ointment should be advised for the patient seen within a few hours of possible exposure. Treatment with several doses of arsphenamin seems to be justifiable for the patient known to be definitely exposed. Success has been reported in several instances with this method. In trying to evaluate this proceeding, however, it should not be forgotten that all exposures are not followed by infection, and entire credit cannot be given to the treatment.

NEW DRUGS

Bismuth.—Within the past year or two, reports either experimental or clinical have been made on several new drugs. While the salts of bismuth have been known for some time to have an effect on syphilis, they have been studied recently by a number of men. As early as 1889, Balzar called attention to their favorable action on certain lesions when injected subcutaneously or intramuscularly. Sazerac and

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Levaditi have studied their effect in the rabbit and in man. They used the tartrobismuthate of sodium and potassium in oil, and recommend a dosage of 0.1 to 0.3 gm. given in courses, so that a total of from 2 to 3 gm. is given in a month. The drug is administered by intramuscular injection. Others who have reported on the use of bismuth are Fournier and Guenot,[1] Jacquet, Marie, Pasini,[2] Duhot.[3] Nearly all agree that the drug has a marked effect on the disease, more on early than on late syphilis, and that care must be exercised in its use. All warn against stomatitis. Duhot states that the kidney should be watched, and that bismuth should not be given in nephritis, tuberculosis or ocular syphilis. Pasini reports on thirty-one cases and states that after two or three doses spirochetes disappear from the lesions and rapid healing follows, although the Wassermann reaction may remain positive. Further work must be done, but it is possible that this drug will have a definite place in cases in which the patient cannot be given the arsenicals.

Sulpharsphenamin.—A product which has been described and made by Voegtlin, Johnson and Dyer[4] of the U. S. Public Health Service under the name sulpharsphenamin, is prepared from arsphenamin, formaldehyd and sodium bisulphite. It contains an average arsenic content of 22 per cent. as compared with arsphenamin 30 per cent. and neo-arsphenamin 18 to 20 per cent., and can be made from any of the arsphenamins, even from lots that appear somewhat toxic. From their experimental work which has been complete, the authors conclude that this drug has certain advantages over neo-arsphenamin: (1) ease of manufacture, (2) great stability of the drug in dry form and in watery solutions, (3) constancy of toxic and parasiticidal action of different lots, and (4) suitability for hypodermic administration. This drug they claim is as well tolerated when injected intravenously as neo-arsphenamin. Intramuscularly it causes some local reaction, but it can be injected subcutaneously with impunity, provided that for full therapeutic doses the concentration is kept high (from 20 to 30 per cent.). Lieut. Commander Powell, U. S. Navy, found a 20 per cent. solution containing from 0.4 to 0.6 gm. injected into the subscapular

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1. Guenot, L., and Fournier, L.: The Treatment of Syphilis by Bismuth Salts, Bull. Soc. franç. de dermat. et syph. **28**:475, 1921.

2. Pasini, A.: Bismuth Preparations in Treatment of Syphilis, Gior. ital. mal. ven. **63**:814 (June) 1922.

3. Duhot, R.: The Treatment of Syphilis by Bismuth Salts, Rev. belg. d urol. et de dermat. syph. **5**:14 (Jan.-March) 1922.

4. Voegtlin, Carl; Johnson, J. M., and Dyer, Helen: Sulpharsphenamine: Its manufacture and Chemotherapeutic Properties, Public Health Rept. **37**:8783 (Nov. 10) 1922.

region to be well tolerated. Much clinical work will have to be done, but the fact that it can be given subcutaneously and that its effect is slow may make it valuable.

Silver Arsphenamin.—Silver arsphenamin is the basis of many reports in the literature, some enthusiastically favorable and some unfavorable. Most reports indicate favorable action on active lesions and on the Wassermann test; generally it gives less reactions than arsphenamin or neo-arsphenamin, but reactions do occur. Because it gave fewer reactions, it was thought that it might be given to patients who had reacted with other arsenicals, but this is unfortunately not borne out. The danger of argyria has kept many from using this drug, but with the many thousands of injections now on record, it is evident that this danger is exceedingly remote. However, if there is the slightest danger, it must be considered carefully before using a drug which carries this agent and has apparently no greater potency than those which do not.

NEW METHODS

Cole, Gericke and Solomon [5] in a preliminary report claim that clinical investigation shows that it is unnecessary in using inunctions of mercury to leave the preparation on for several days. If this is true, and if the patient can bathe after rubbing the drug in well, it will do away with much of the disagreeableness of an effective method of using mercury.

Eicke and Rose have experimented with a combined solution of neo-arsphenamin and mercury sublimate. They prepare it by adding 1 c.c. of a 1 per cent. sublimate solution to from 2 to 5 c.c. of distilled water in which they dissolve the neo-arsphenamin. This is injected intravenously. Pezolt gave 3,700 injections; 378 patients had a positive Wassermann reaction; of 251 subsequently tested, ninety-six gave a negative reaction at the end of the course of treatment. At the end of three months, fifty-eight were still positive.

Dennie and McBride [6] report good results in the treatment of arsphenamin dermatitis with intravenous injections of a solution of sodium thiosulphate. The drug is used in doses of 0.3, 0.45, 0.6 and 0.9 gm. daily and then 1.2 gm. on the sixth day and 1.8 gm. on the eighth day. I have had verbal reports from others on the usefulness of this drug in shortening this unfortunate complication.

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5. Cole, H. N.; Gericke, A. J., and Solomon, T.: The Clean Inunction Treatment of Syphilis with Mercury. Preliminary Report, J. A. M. A. **77**:2022 (Dec. 24) 1921.

6. McBride, W. L., and Dennie, C.: Treatment of Arsphenamin Dermatitis and Certain Other Metallic Poisonings, Arch. Dermat. & Syph. **7**:63 (Jan.) 1923.

Fordyce[7] and Rosen have made use of a solution of mercuric chlorid in palmetin, particularly in treating congenital syphilis. It can also be used in adults, and on account of the slow absorption a dose of from 1 to 1.5 grains (0.06 to 0.09 gm.) can be given intramuscularly once a week. There is practically no pain.

ABORTIVE TREATMENT

The present day literature does not show many enthusiasts for what was formerly considered good abortive treatment, namely, a few injections of one of the arsenicals given in a few weeks' time.

E. Freund,[8] writing on "Abortive Treatment," states that recent cases of Wassermann negative syphilis may be aborted with one course of arsphenamin and mercury, but at least two or three courses should be given. Meirowsky and Leven[9] hold that no matter whether the Wassermann test is positive or negative, even the earliest symptoms should be treated with two or three courses of arsphenamin and mercury. Mulzer reports an increase in reports of failure in attempted abortive treatment.

There is general agreement that if such treatment is to be undertaken, it should be only in cases positive for spirochetes and with a negative Wassermann reaction that doses of arsphenamin should be large and given at frequent intervals—mercury should be included in the treatment—and that at least a second course should be given. One very important point is the frequent testing of the blood, since some patients who are at first negative become positive after treatment starts, and if this happens, the case should not be considered as in the "abortive" class.

The treatment recommended by Fordyce is fairly typical. In cases classified as above, he recommends eight injections of arsphenamin—0.3 to 0.5 gm. each (dosage according to sex, weight, and age of patient). The first three injections are given every other day in vigorous persons who tolerate the drug well, and the remaining doses every five to seven days. A second course of six injections is given after an interval of from four to six weeks. Some men suggest that the first three doses be given daily; more, however, prefer every other day. Some will give injections of mercury either on days between the arsphenamin injections or in the interval of rest between the courses of arsphenamin. Such patients should be under careful observation

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7. Fordyce, John A.: Treatment of Syphilis, in Venereal Disease.—Information Issued by U. S. Public Health Service **4**:112.

8. Freund, E.: Abortive Treatment of Syphilis, Gior. ital. d. mal. ven. **63**:316 (May) 1922.

9. Meirowsky and Leven: Principles in the Abortive Treatment of Syphilis, München. med. Wchnschr. **68**:106, 1921.

for at least a year, monthly tests being made. If the classification is rigidly adhered to and a sensitive antigen used, not many favorable cases will present themselves. It should be carefully noted that practically all syphilologists are agreed that not less than from twelve to fourteen doses of arsphenamin combined with mercury should be given and treatment carried on for at least from four to six months.

SECONDARY SYPHILIS

So far as treatment is concerned, I would include here not only the usual case with skin eruption, but also the chancre with a positive Wassermann reaction.

In undertaking the treatment in a case of early syphilis, every means should be used to clinch the diagnosis to the satisfaction not only of the physician, but of the patient as well. There are still too many physicians starting treatment on a diagnosis based on questionable symptoms; I mean by this an initial lesion in which diagnosis is made clinically only, either with or without a Wassermann test, a case in which diagnosis is based on a single positive Wassermann test or in some cases even on a single partly positive Wassermann test. This is a practice that cannot be condemned too emphatically. Syphilologists are too frequently called on later to try to untangle such a case and advise the patient as to what should be done. The patient's reactions at this time may be entirely negative with only a questionable history to go on, and one is in a quandary as to whether his reactions have been made negative by treatment or not. It is a serious matter to advise any one to continue for two or three years a treatment that is expensive, not without some danger and possibly entirely unnecessary, and yet one does not lightly assume the responsibility of possible serious recurrences if treatment is not advised. Therefore the first step in treatment should be a complete examination which will include examination for spirochetes if a lesion is present, a blood test performed with at least two antigens, and either repeated or examined at different laboratories. Such an examination may not only disclose additional evidences of syphilis, but possible contraindications to one or the other type of treatment. There should be frequent examinations of the urine; this simple matter is frequently omitted, and later albumin is found, and one does not know whether it was present previously, or whether it is a result of the disease or of the treatment. Once a diagnosis is established and the patient is satisfied it is correct, time should be taken to go over the entire situation carefully with him, outlining in a general way the complete treatment—its cost, etc. To me, starting treatment on a case with the statement that the patient has a "blood infection" or a touch of "the old ral," is nothing short of criminal. Under such circumstances, a patient practically never takes enough treatment to

amount to anything, and it has been just such practice in the past that has given us the number of cases of late syphilis that we see today. During 1922 approximately 75 per cent. of the cases reported in Minnesota were late syphilis, and I believe a majority of them are due to the physician's negligence in handling the case properly when the diagnosis was first made.

There has been much talk of a so-called standardized treatment of syphilis, and outlines for such treatment were published for the Army and Navy, by the U. S. Public Health Service and by many state boards of health. In a way, these have been valuable, but they have also been productive of harm, as many men have accepted them literally and applied them to all cases without discrimination. One may suggest certain standards by way of the minimum amount of treatment to give in certain classified cases, but to attempt to treat a disease so varied in its attack as syphilis by any one method, is to one who has had experience quite impossible. This sort of thing has given the uninformed and inexperienced physician a degree of confidence in treating syphilis that he should not enjoy, and the results are manifest more or less frequently. While a number of new drugs have been mentioned, I believe the use of them should still be limited to experienced men who are doing a large amount of clinical and experimental work, and that generally we should confine ourselves to the well established drugs—arsphenamin, neo-arsphenamin, mercuric salicylate, mercuric chlorid, mercury succinimid, mercurial ointment and potassium iodid.

As to the choice between arsphenamin and neo-arsphenamin, no clinical work has been done which definitely proves one or the other drug more potent. Schamberg [10] claimed by experimental work that the therapeutic index of neo-arsphenamin is higher. On the other hand, it has been shown that arsphenamin is more stable and more uniform. Neo-arsphenamin is not uniform in its action in all lots; it is not stable; it may deteriorate in the ampule, and it is easily affected by slight errors in technic. Yet without question neo-arsphenamin is used in the great majority of instances. I feel that there is no great difference in their general therapeutic effect. There is considerable debate as to a dosage to be used; many believe that best results, particularly in early cases, can be obtained only by using the maximum dose of 0.6 gm. arsphenamin and 0.9 gm. of neo-arsphenamin. On the other hand, it is claimed such doses produce no better effect than the average dose of 0.4 gm. of arsphenamin and 0.6 gm. of neo-arsphenamin, and that the larger doses definitely increase

10. Schamberg, J. F.; Raiziss, G. W., and Kolmer, J. A.: Chemotherapeutic Consideration of Pentavalent Trivalent Arsenic, J. A. M. A. **78**:402 (Feb. 11) 1922.

the danger of reactions. This point of dosage cannot be arbitrarily settled; no doubt there are times when the larger dosage should be used, and I believe there is also no doubt that the small dosage (less than those mentioned), even if repeated at shorter intervals, is often inefficient. Klauder's recent experimental work (paper read at the American Dermatological meeting) tends to show that repeated small doses tend to lessen the effect of later treatment. Certain it is that in early syphilis much may be gained by intensive treatment, and in these cases, if in any, large doses are justifiable. It is, however, wise always to start with a small dose.

It is unnecessary to go into technical details of treatment. The various manufacturers' advice as to preparation of the drug should be followed in detail.

In cases in which there are no infectious lesions, some prefer to give a course of mercury first, with the idea that the disease is established and two or three years of treatment must be given; that the mercury permits the patient to produce his natural immunity as it does not quickly kill off the spirochetes which are stimulating this function, and that it prepares the way for arsphenamin. When there are infectious lesions, most physicians give arsphenamin first, although even in these cases it is recommended that a dose or two of mercury be given first. Most physicians give eight injections of the arsenicals in the first course, usually giving a small dose to begin with and frequently giving the first three doses with only a day between, then giving the remaining doses at weekly intervals. The rest periods in the first year are from four to six weeks; personally, I do not allow these periods to exceed four weeks without some special reason. I have recently talked with a number of syphilologists, and I believe that the tendency is increasing to treat patients with established cases for a minimum of two or three years regardless of negative serologic findings. In the second year in favorable cases, the rest periods may be extended to two months and possibly three. Personally, I like to give at least two courses of mercury in the third year, several months apart.

Under this general outline, a patient receives not less than from twenty to twenty-five doses of the arsenicals and not less than five or six courses of mercury, either injections or inunctions, during a two to three year period. This constitutes what might be called a standard of minimum treatment in average cases, and is in accordance with my own experience and that of a number of other experienced syphilologists. Potassium iodid is not used much nowadays in early syphilis, although many physicians like to give it during the periods of rest from active treatment. Wassermann tests should be made at intervals and should include the cholesterolized antigen and Kolmer technic, since these are more slowly influenced by treatment.

CURE

While I believe there are some patients with syphilis who get well with almost no treatment, and those who become well after what seems a small amount of treatment, there is at the present time no method of classifying these cases. I am therefore convinced that in order to be reasonably sure of curing our patients, we must subject all of them to what is required in the most severe case (not including the occasional malignant case)—treat them all over a minimum of two or three years. There should be an observation period of at least two or three years, during which blood and finally, at least, spinal fluid tests should be made; it may be that this period should be extended indefinitely.

CONCLUSIONS

Every patient should be completely examined and his condition positively diagnosed before treatment is undertaken. Abortive treatment should be undertaken only in carefully selected cases, and even then two or three courses of both mercury and arsphenamin should be given.

Methods of treatment are now pretty well settled as to minimum requirements, but this treatment should extend in all cases over a two or three year period regardless of favorable serologic findings, and should include the arsenicals and either injections or inunctions of mercury.

Our problem is to convince the patient of the need of this extended treatment and to assume some responsibility in seeing that it is given.

There should be a period of at least two or three years of observation after treatment, and occasional late relapses indicate that this may well be even further extended.

601 Syndicate Building.

DISCUSSION

Dr. Harry E. Alderson, San Francisco: Dr. Irvine brings out very well the fact that early diagnosis and prompt, vigorous treatment, intelligently directed, offers the best hope for cures. The matter of deciding when a syphilitic person is rid of his disease is still unsettled. It must be remembered that the first Wassermann reaction dates back only seventeen years, and there have been numerous modifications since then. The first arsphenamin injection was given only sixteen years ago, and this generation probably will not see the question settled. It can be said that the greatest responsibility rests with the physician who first sees the early cases.

Dr. Ernest Dwight Chipman, San Francisco: Along the line of therapy it has been amply brought out that what we should keep in mind is that in syphilis, as in all disease, we must remeber the maximum, "Treat the patient and not the disease alone." We must give drugs relentlessly at some times to get their physiologic effect, but at other times we must employ the same agents with caution and determine our future action by the reactions observed.

DR. H. M. GREENE, Portland, Ore.: If syphilis is cured by polypharmacy, it is an exception to the rule. Some drugs are synergistic in their action, while others are incompatible, and from the experimental work of Schamberg and his associates, we have proof of the physiologic incompatibility of mercury and arsenic. Mercury irritates the kidney and not only inhibits the elimination of arsenic, but also normal body waste as well; while arsenic produces a similar detrimental effect on the liver, the organ on which we depend materially for the elimination of mercury. If we combine these two remedies and use them conjointly in treating syphilis, mercury prevents the kidney from eliminating arsenic, and arsenic prevents the liver from eliminating mercury. The result is an intoxication of the patient by the accumulation of both mercury and arsenic which cannot build up his resistance or cure his disease by direct action of the drugs. Mercury is a resistance building drug, has low spirocheticidal action, and its use should be reserved for the last part of the treatment. Especially in early cases, arsenicals should be used at maximum dosage on account of their high spirocheticidal action, the highest of any drug yet discovered. First doses should be small in every case to prevent an untoward action of the remedy. If neo-arsphenamin is the drug of choice, give 0.3 gm.; if there is no severe reaction, in three days give 0.45 gm., followed in five days by 0.6 gm.; and in one week 0.75 gm. Within from twenty-four to seventy-two hours after the first dose the chancre and mucous patches will usually be free from spirochetes, and it may be presumed that the blood has been cleared of the organisms also. After the patient is clinically well, further treatment is to be directed against the resting forms of the germ, and the interval between doses may be prolonged to three or four weeks, as the life cycle of the spirochete appears to be twenty-one days approximately; that is, twenty-one days from exposure until the chancre appears, twenty-one days for the chancre to develop, and twenty-one days for secondary manifestations to appear. Give eight to ten doses in the first course, or a total of from 8 to 10 gm. of neo-arsphenamin, with iodids by mouth. When there is good toleration for the remedy, and the patient weighs 100 kilograms, a dose of 1.5 gm. can be administered without any unfavorable reaction.

DR. L. G. ROWNTREE, Rochester, Minn.: Despite any theoretic ideas to the contrary, it seems to me that the logical thing to do is to follow a multiple plan of attack in the treatment of syphilis at the earliest possible moment after diagnosis and to force that treatment along the lines so well presented by Dr. Irvine. I know he has been a leader in the follow-up treatment of syphilis in this country, and it seems to me that is the second thing in the treatment of syphilis.

DR. WALTER V. BREM, Los Angeles: I wish to emphasize a thought that has been advanced by several speakers—that the problem is one of treatment of the patient rather than of the disease. We are too prone to outline what we call courses of treatment and to attempt to institute these in almost every instance. We have all seen patients that gave a history of syphilis that we could scarcely doubt, and who had received long years before inadequate treatment, but with a negative Wassermann reaction and no signs of syphilis. We have all had patients that responded quickly to treatment and others in whom no impression was manifested serologically no matter how vigorously we applied treatment. That applies to the treatment over a long time. Each case must be considered individually, and we can only tell about subsequent treatment by repeated observation and serologic tests.

Dr. Solomon Solis Cohen, Philadelphia: There is no question more important than the treatment of syphilis. As typhoid fever is the typical field for the exercise of therapeutic judgment in acute infections, so is syphilis in chronic infections, and we cannot approach the question of the treatment of syphilis without recognizing that it is a chronic infection and that although the treatment is directed against that infection in a particular patient and modified by the individual reactions of that patient, nevertheless it is a treatment of a definite infection running a more or less definite course. It is not right or fair to say that we are to treat not the disease but the patient: we are to treat the disease in the patient. Anything less is one of these dangerous half truths that lead to disaster. Recognizing that we have this form of chronic infection in persons with peculiarities, we have to go further and recognize that we are dealing with three variants: the particular strain of spirochetes with which the patient may be infected and their virulence, the resistance of the patient and specific proclivities. That there are special strains of spirochetes, different strains, and that these differ not only in their relative virulence but also in their selective affinities for different tissues, I think the whole course of clinical medicine and the large part of pathologic data go far to prove.

In regard to the important question of mixed treatment in syphilis, its value cannot be questioned. The teaching that we are to depend on a single agent is dangerous, and I cannot hear this said without contradicting it. I remember before the introduction of arsphenamin when we had to depend on mercury and potassium iodid used cito, tuto, jucunde. The indications are just the same with arsphenamin. Unfortunately, we have no mathematical standard, and we have to fall back on that very fallacious instrument, clinical judgment, but if we cannot trust our clinical judgment in syphilis or anything else we have no right to practice medicine but should go into research laboratories and study. Persist in the treatment; that does not mean for three months or six months or two years, but throughout the life of the patient, and our courses of treatment through these years are to be watched.

Dr. Harry G. Irvine, Minneapolis: I had occasion to review a series of cases treated after a five year period, and while it was not possible to get in touch with many of the patients, we had the impression that the patients treated early in the disease had remained clinically and serologically free during these years. This makes it necessary to emphasize the need of treating these patients in the early stages of the disease; if this can be done by physicians in general practice, it will reduce materially the incidence of the disease. I think from what Dr. Green started to say that he is in favor of attempting to cure syphilis by arsenicals alone. If this is the case, he stands almost, if not entirely, alone. The literature contains many reports of cases in which arsphenamin alone has been tried, and when these cases have been reviewed after several years, it has been found that there were many more relapses than in those cases in which mercury also was used. Yesterday at the clinic Dr. Ormsby and Dr. Montgomery both emphasized the use of mercury in the treatment of syphilis. Dr. Montgomery said that the French had a large number of patients treated by arsenic only and another group had been treated by mercury only during the war. These men were sent to the front and were away for a year; a large number were then reexamined. Those treated with mercury whose tests were negative at the time of treatment were still negative, and those whose tests were partly negative were still about the same. On the other hand, half of those who had received arsenic only showed a reversion to a positive Wassermann test. I wish to emphasize that at the present time it is

dangerous to advocate the treatment of syphilis by arsenic only. I also believe that it is dangerous to advocate the use of extremely large doses of arsphenamin. Dr. Ormsby yesterday emphasized the fact that we should begin with a small dose, and I think he does not use large doses at any time. Many of the unfavorable reactions are due to the large doses. It may be possible that some time in the future it can be shown that we can cure syphilis by arsphenamin only, and that mammoth doses can be given without injury to the patient; but I think that this is not true at present.

HISTOLOGIC CHANGES PRODUCED EXPERIMENTALLY IN RABBITS BY THE IODIDS OF POTASSIUM AND SODIUM *

JOHN A. KOLMER, M.D.
AND
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PHILADELPHIA

In previous papers, we have reported the results of studies on the histologic changes produced experimentally by the administration of arsphenamin,[1] neo-arsphenamin,[2] mercury [3] and bismuth.[4] The results have shown that these compounds in certain amounts may produce degenerative effects in some of the internal organs, notably the liver, by arsphenamin and the kidneys by neo-arsphenamin, mercury and bismuth. Since investigations of this kind have proved of value and interest clinically in relation to the chemotherapy of syphilis, and since the iodids are frequently used in conjunction with these substances, a similar study was undertaken to determine their effect on certain organs, that is, the brain, heart, lung, spleen, suprarenal glands, kidney and liver. Investigation on the action of the iodids appears to have been confined largely to clinical and functional studies. We were able to find but few references to previous morphologic work on the organs to be reported on.[5]

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* From the Research Institute for Cutaneous Medicine and the McManes Laboratory of Pathology, University of Pennsylvania.

1. Kolmer, John A., and Lucke, Baldwin: A Study of the Histologic Changes Produced Experimentally in Rabbits by Arsphenamin, Arch. Dermat. & Syph. **3**:483-514 (April) 1921.

2. Kolmer, John A., and Lucke, Baldwin: A Study of the Histologic Changes Produced Experimentally in Rabbits by Neo-Arsphenamin, Arch. Dermat. & Syph. **3**:515-530 (April) 1921. A Comparative Study of the Histological Changes Produced Experimentally in the Liver and Kidneys of the Rat by Arsphenamin and Neo-Arsphenamin. Ibid. (being published).

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5. Boehm, R.: Beitrage zur Pharmakologie des Jods, Arch. f. exper. Path. u. Pharmakol. **5**:329, 1876. Sgalitzer, M. V. C.: Kritische Versuche zur Kodalkaliwirkung, Arch. internationales de Pharmacol. et de Therap. **18**:285, 1908.

EXPERIMENTAL

Rabbits, kept under standard conditions, were used in all experiments. Chemically pure potassium or sodium iodid, dissolved in 5 c.c. of water, in single or multiple doses ranging from the equivalents of the usual therapeutic amounts to several times those quantities, were administered daily or twice weekly by the stomach tube or intravenously (Table 1). The weight of the animals was noted after each injection.

Results of Injections of Potassium and Sodium Iodid into Rabbits

Rabbit No.	Type of Compound	Route of Administration	Dose per Kg. in Grams	Time Interval of Injections	No. of Doses	Weight at Beginning of Treatment in Grams	Weight at Completion of Treatment in Grams	Results
24	KI	Stomach	0.04	Daily	19	1,710	1,650	Died
15	KI	Stomach	0.04	Daily	36	1,570	1,400	Killed
14	KI	Stomach	0.08	Daily	36	2,045	1,940	Killed
26	KI	Stomach	0.08	Daily	23	2,100	1,710	Died
35	KI	Stomach	0.12	Daily	36	1,665	1,700	Killed
29	KI	Stomach	0.12	Daily	28	1,970	1,545	Died
31	KI	Stomach	0.24	Daily	36	1,800	1,875	Killed
33	KI	Stomach	0.24	Daily	36	1,900	2,090	Killed
38	NaI	Stomach	0.04	Daily	24	1,470	1,420	Died
36	NaI	Stomach	0.08	Daily	26	1,920	1,800	Died
40	NaI	Stomach	0.12	Daily	27	2,000	1,495	Died
39	NaI	Stomach	0.24	Daily	22	1,950	1,855	Died
41	KI	Intravenous	0.02	Twice weekly	12	1,725	1,555	Killed
42	KI	Intravenous	0.04	Twice weekly	12	1,700	1,550	Killed
43	KI	Intravenous	0.06	Twice weekly	6	1,780	1,460	Died
44	KI	Intravenous	0.10	Twice weekly	12	2,100	1,255	Killed
46	NaI	Intravenous	0.04	Twice weekly	7	2,090	1,685	Died
47	NaI	Intravenous	0.08	Twice weekly	12	2,880	1,790	Killed
48	NaI	Intravenous	0.16	Twice weekly	3	3,180	3,170	Died
20	KI	Intravenous	0.10	.....	1	1,840	.....	Killed
30	KI	Intravenous	0.15	.....	1	2,000	.....	Killed
23	NaI	Intravenous	0.10	.....	1	1,630	.....	Killed
27	NaI	Intravenous	0.20	.....	1	2,260	.....	Killed
32	NaI	Intravenous	0.50	.....	1	1,885	.....	Killed

Of the twenty-four rabbits employed, ten died before the entire series of treatments planned was completed; necropsies were performed on these a few hours after death. The animals that received repeated doses and survived the entire course were killed by decapitation on the day following the completion of the series; the animals that were injected with a single dose were killed five days after the injection. Sections from the following organs were prepared (solution of formaldehyd U.S.P., paraffin, hematoxylin-eosin) and studied histologically: brain, heart, spleen, suprarenal glands, lung, kidney and liver.

HISTOLOGIC CHANGES PRODUCED BY MULTIPLE DOSES OF POTASSIUM IODID ADMINISTERED ORALLY

Potassium iodid was administered to rabbits daily by a stomach tube; from nineteen to thirty-six doses of from 0.04 to 0.24 gm. per kilogram of weight were given (Rabbits 24-33). These amounts corresponded to approximately from 2.5 to 15 gm. per 60 kilograms.

No tissue changes were found in the brain, heart and suprarenal, and slight alterations only were observed in the lung, kidney, liver and spleen. They are briefly summarized as follows:

Kidney.—In the animals surviving the thirty-six doses, the changes were slight. There were no demonstrable differences between those receiving the smaller and those receiving the larger amounts of the compound. The vessels were generally not engorged, but they contained an unusual amount of serum. Where erythrocytes were present they were well preserved. The glomeruli were normal in size; their capsules were delicate; the capsular lining was flat; no foreign contents were generally present in the capsular space, although occasionally some granular albuminous precipitate was seen. The tufts had the average number of nuclei; these stained well, and they were of normal size and shape. The glomerular coils were usually not engorged; some loops were filled with serum only; elsewhere normally preserved erythrocytes were present. In the lumina of many of the tubules there was a moderate quantity of hyaline or granular eosin staining precipitate. The epithelium of the convoluted tubules was usually slightly swollen, and finely or coarsely granular; the nuclei were well preserved. The thick limbs of Henle showed a granular condition, the thin limbs and the collecting tubes had a normal lining. The animals which did not survive the full course showed somewhat marked changes, particularly in the cells of the convoluted tubules, and to a lesser extent in those of the ascending limbs. The epithelium was more swollen, granular and sometimes finely vacuolated; many cells were devoid of their nuclei.

Liver.—In some of the animals surviving thirty-six doses, the periportal connective tissue was moderately cellular and increased in amount; the cellularity was due to the presence of deep staining, short, oval connective tissue nuclei. With the exception of some lymphocytes, no foreign cells were present. The portal canals and the bile ducts were normal. The interlobular capillaries and the central lobular veins were slightly engorged, often with an excess of serum, rather than with erythrocytes. The liver cells, on the whole, were in a good state of preservation, but occasionally a slight increased granularity was seen. In a few animals only, particularly in those that died before the completion of the course of treatment, the cells in the central portion of the

lobules were either coarsely granular or appeared quite smooth, and they contained numerous clear-cut, small fat vacuoles, as well as less clearly outlined, lightly eosin-staining droplets. Necrotic cells were not encountered. Some slight bile pigmentation was now and then seen.

Lung.—The vessels were moderately engorged, and a few air sacs were flooded with serum. The nuclei of the capillary endothelium was unaltered. The bronchi occasionally contained some granular eosin-staining substance; a few of their lining cells showed an excess of mucoid material. Foreign cells were present only in some of the animals dying before completion of the course.

HISTOLOGIC CHANGES PRODUCED BY MULTIPLE DOSES OF SODIUM IODID ADMINISTERED ORALLY

Sodium iodid was administered to rabbits daily by stomach tube, from twenty-two to twenty-seven doses of from 0.04 to 0.24 gm. per kilogram of weight were given (Rabbits 38 and 39). All of the animals died after receiving twenty-two doses. These amounts likewise corresponded to approximately from 2.5 to 15 gm. per 60 kilograms of weight. The results have been summarized as follows:

Kidney.—The tissue changes were similar to those of the preceding group, namely, the cells of the convoluted tubules and, to some extent, those of the ascending limb were swollen, granular and here and there finely vacuolated. Some of the nuclei stained poorly, and occasional cells were anuclear. The glomeruli showed nothing of note. The vessels contained an unusual quantity of serum.

Liver.—The periportal connective tissue, the portal canals and the bile ducts were normal. The cells in the central two thirds of the lobules, especially in the animals which had received twenty-two doses of 0.24 gm. per kilogram, were somewhat swollen, indistinctly outlined, and packed with numerous clear-cut fat vacuoles, or less clearly outlined eosin-staining droplets. Some nuclear shrinkage or paling was present. In brief, the changes were identical with those of the potassium iodid group.

Lung.—The vessels were somewhat engorged, and a few of the alveoli were filled with a hyalin material. Here and there small collections of polymorphonuclear leukocytes were found. In the bronchial mucosa, there was a slight excess of mucous secretion.

HISTOLOGIC CHANGES PRODUCED BY MULTIPLE DOSES OF POTASSIUM IODID ADMINISTERED INTRAVENOUSLY

Potassium iodid was injected intravenously twice weekly for from six to twelve doses of from 0.02 to 0.10 gm. per kilogram of weight

(Rabbits 41 to 44); these amounts corresponded to approximately 1.2 to 6 gm. per 130 pounds (58.96 kg.). One animal (No. 43) died after six doses and showed somewhat more marked changes than the other animals which survived twelve doses. The tissue alterations were slight and in no instance well defined. The histologic changes were as follows:

Kidney.—The interstitial tissue was unaltered. The vessels were not engorged, had normal walls and contained an excess of serum. The glomeruli were of normal size, capsules delicate and capsular lining flat; there were no foreign contents in the capsular spaces. The tufts were normally nuclear, and their coils were filled with well preserved erythrocytes. The tubules contained moderate amounts of granular or hyaline eosin-staining precipitates. The epithelium of the convoluted tubules was slightly swollen, frequently finely and coarsely granular, and in the animal which died showed fine vacuoles. The nuclei were generally preserved. The ascending limbs of Henle showed a somewhat similar condition. The descending limbs and the collecting tubules were normal.

Liver.—The periportal connective tissue was normal; there were no changes in the bile ducts or portal canals. The contents of the vessels were often hyaline. The interlobular capillaries were generally not engorged. The liver cells in the central portions of the lobules were at times slightly swollen, granular and filled with numerous clear-cut vacuoles or ill defined eosin-staining droplets. The cells at the lobular peripheries were unaltered.

Lung.—A slight congestion and occasional flooding of some air sacs with serum marked the general condition. In the animal which died before the completion of the twelve injections, small collections of leukocytes were sometimes encountered.

Spleen.—Moderate amounts of hemosiderin granules were scattered throughout the pulp. Most of the pigment was engulfed by mononuclear phagocytes. There was no change in the connective tissue or the follicles.

HISTOLOGIC CHANGES PRODUCED BY MULTIPLE DOSES OF SODIUM IODID ADMINISTERED INTRAVENOUSLY

Sodium iodid was injected intravenously twice weekly for from three to twelve doses of from 0.04 to 0.16 gm. per kilogram of weight (Rabbits 46 to 48). These amounts corresponded to approximately from 2.5 to 10 gm. per 130 pounds of weight.

The microscopic changes in the kidneys, liver, lung and spleen were essentially similar to those of the preceding potassium iodid group.

HISTOLOGIC CHANGES PRODUCED BY SINGLE DOSES OF POTASSIUM IODID AND SODIUM IODID INTRAVENOUSLY

In addition to these, rabbits were given single intravenous injections of potassium iodid in doses ranging from 0.1 to 0.15 gm. per kilogram of weight; these amounts were about one third of the maximum tolerated dose by intravenous injection and corresponded to approximately from 6 to 10 gm. per 60 kilograms, or 130 pounds. Rabbits were also given single intravenous injections of sodium iodid in doses of from 0.1 to 0.5 gm. per kilogram, which were from one-fourth to one-twentieth of the maximum tolerated doses and corresponding to approximately from 6 to 30 gm. per 60 kilograms, or 130 pounds. Tissue changes were not produced in any animals of these two groups.

SUMMARY

The histologic changes produced experimentally in rabbits by the iodids of potassium and of sodium are reported.

One group of twelve animals received daily by stomach tube from 0.04 to 0.24 gm. of potassium or sodium iodid per kilogram of body weight; these amounts were equivalent to from 2.4 to 14.4 gm. per 60 kilograms (weight of adult man). Five animals survived the full course of thirty-six doses; the others died after from nineteen to twenty-eight administrations. Nine animals lost weight, three gained up to about 200 gm. of weight. The tissue changes found were inconspicuous and occurred only in the lung, kidney and liver. These changes consisted of a slight pulmonary congestion with traces of edema, an equally slight cloudy swelling of the convoluted tubules and of the ascending limbs of Henle in the kidneys, and a cloudy swelling with slight fatty and hydropic changes in the central parts of the hepatic lobules. In addition, the vessels within these and other organs contained an unusual amount of clear serum. Individual animals exhibited varying degrees of resections, but in general the difference in dosage or in compound did not produce essential differences in the character of the histologic changes. The lesions, always slight, were a little more definite in the animals that died before the completion of the entire series. The periportal changes described in the liver were probably spontaneous, since they occurred also in a number of control rabbits.

A second group of seven animals received intravenously, twice weekly, from 0.02 to 0.16 gm. of potassium or sodium iodid per kilogram of body weight. These amounts were equivalent to from 1.2 to 9.6 gm. per 60 kilograms. Four animals survived the full course of twelve injections; the others died after from three to seven injections. All of the rabbits lost weight. The tissue changes were inconspicuous and resembled in all details those of the preceding group, except that

in several animals the spleen showed moderate hemosiderin depositions. The difference in dosage and compound did not produce any essential differences in the histologic picture.

The third group of five rabbits received a single intravenous injection of from 0.1 to 0.5 gm. of sodium or potassium iodid per kilogram of body weight; these amounts were equivalent to from 10 to 30 gm. per 60 kilograms. Three of these animals did not exhibit any general symptoms after the injection; the remaining two presented a temporary reaction with recovery in an hour. Five days after the injections the animals were killed; no tissue changes were found.

CONCLUSIONS

1. Administration to rabbits by stomach tube of potassium and sodium iodid in repeated large doses equivalent to approximately as much as 15 gm. per 60 kilograms of body weight, and repeated intravenous injections in amounts approximately equivalent to as much as 1 gm. per 60 kilograms as well as single intravenous injections in amounts equivalent to approximately 30 gm. per 60 kilograms, did not cause tissue changes in the brain, heart, and suprarenals. The kidney, liver, lung and spleen showed slight tissue reactions which may be interpreted as the result of a mild irritation.

2. Dosage, compound and route of administration did not produce any essential differences in the histologic changes.

3. These findings are in marked contrast to the well defined degenerative lesions produced by arsenic, mercury and bismuth.

Abstracts from Current Literature

THE VALUE OF THE KAHN PRECIPITATION TEST FOR SYPHILIS. H. K. DETWEILER, J. A. M. A. **81**:815 (Sept. 8) 1923.

This report from the Toronto General Hospital gives the results of 1,540 parallel Kahn and Wassermann reactions. There was agreement in 94.2 per cent. of the tests. Where there were discrepancies, the evidence favored the Wassermann test in the majority of instances. The Kahn test was found to be not as reliable as the Wassermann reaction, particularly in early primary, treated and cerebrospinal syphilis. However, the Kahn test is much simpler, and in the Toronto General Hospital both tests are now being performed.

FOOD ALLERGY AS A CAUSE OF ILLNESS. W. W. DUKE, J. A. M. A. **81**:886 (Sept. 15) 1923.

After discussing the general considerations which underlie the phenomena of allergy, the author mentions the symptoms which occur in this disease. They are numerous and may affect any region or system of the body, the most common, however, being referable to the gastro-intestinal and bronchial tracts and to the skin.

Symptoms referable to reactions to foods are divided into contact and general reactions, dependent on whether the noxious substance produces a local effect or acts after its absorption. Asthma and hay-fever are more commonly of the former type, urticaria of the latter.

Dermal and intradermal tests are useful aids in diagnosis. In food cases, skin tests, especially cutaneous tests, often fail completely. Group testing has certain advantages.

In the treatment of food allergy, avoidance of the allergy substance is the method of choice. Specific protein treatment for food sensitivity is often ineffective.

HODGKIN'S DISEASE AND LYMPHOSARCOMA: A CLINICAL AND STATISTICAL STUDY. A. U. DESJARDINS and F. A. FORD, J. A. M. A. **81**:925 (Sept. 15) 1923.

The authors present data derived from the Mayo Clinic records between the years 1915 and 1920. This is part of a study to determine the effect of systematic irradiation treatment as now practiced.

The clinical manifestations of the two diseases show a close parallelism. Toxic pruritus occurs somewhat more frequently in Hodgkin's disease (9 per cent. of 135 cases) than in lymphosarcoma (3 per cent. of 102 cases). Other skin manifestations were occasionally encountered; two cases of diffuse bronzing are mentioned. In seventy-three cases of Hodgkin's disease the average duration of life was two years and seven months; in fifty-five cases of lymphosarcoma, two years and five months.

MICHAEL, Houston, Texas.

FACTORS CONCERNED IN THE PRODUCTION OF LESIONS OF THE EYE IN EXPERIMENTAL SYPHILIS. WADE H. BROWN and LOUISE PEARCE, New York State J. M. **23**:376 (Sept.) 1923.

The authors review the causes for variation in the results of syphilitic infection and, while admitting that different strains of the organism may show predilection for special parts of the body, they point out also that a single strain may be changed in its character by varying the conditions of passage through the animal body. If transfers are made during the period of active lesions the strain tends to remain active or even become more virulent, while if transfers are made while the disease is latent, the strain tends to lose a certain amount of its pathogenic quality. The point of inoculation also has its effect on the virulence of the resulting infection, partly on account of the adaptation of the part to the nutritive requirements of the spirochete, partly on account of the local or general resistance which can be brought to bear at the point of infection. Females are ordinarily more resistant than males, and the pregnant female is ordinarily more resistant than the nonpregnant female. The authors admit that certain organisms are more prone to produce lesions of the eye than are others, but they doubt whether this tendency can be attributed to any special affinity for the eye. On the other hand, they believe that it is more likely that manifestations of this kind are referable to some peculiarity in the reaction which these organisms arouse or in their resistance to ordinary processes of control.

WILLIAMS, New York.

EXPERIMENTAL XANTHOMA IN RABBITS. M. CHUMA, Virchow's Arch. f. path. Anat. **242**:275 (April) 1923.

By feeding hydrous wool fat to rabbits over a period of 300 days, Chuma induced a generalized yellowness and thickening of the skin, and nodules developed, some as large as a cherry stone. The skin became wrinkled and lost its elasticity. The hair became lustreless and much of it fell out on the neck, belly and extremities. The histology was good for human xanthoma tuberosum, and all of the appendages were atrophic. After injecting carmin into the skin, he found that it became phagocytized by "histiocytes" which contained also fat globules and doubly refractive fat granules, which stained with Sudan III. He concludes from all this that at least some of the pseudoxanthoma cells have their origin in fibroblasts, and that xanthoma of man is induced by the local stimulus of a persistent hypercholesterolemia. He also describes in detail the cholesterol deposits in the internal organs, the eye, the tongue and the joints.

WEIDMAN, Philadelphia.

DERMATOLOGIC ABSTRACTS

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

ETIOLOGY AND TREATMENT OF HERPETIC (APHTHOUS AND APHTHO-ULCERATIVE) STOMATITIS AND HERPES LABIALIS. H. J. GERSTENBERGER, Am. J. Dis. Child. **26**:309 (Oct.) 1923.

Gerstenberger found that the administration of the water soluble B vitamin produces in herpetic stomatitis, aphthous stomatitis, herpes labialis, acute gingivitis, and ulcerative stomatitis a remarkably rapid improvement and

recovery. It is suggested that the primary etiologic factor in these cases is metabolic and nutritional, and that any rôle that bacteria or similar agents may play in the future development of the local lesions is secondary. This metabolic disturbance may be due to a disproportion between the water soluble B supply of the body and the metabolic requirements of the patient for this vitamin at a given time. The constant and liberal use of canned tomato is advocated as an economic and dependable source of the water soluble B vitamin.

TOXEMIA OF SEVERE SUPERFICIAL BURNS. B. Robertson and G. Boyd, J. Lab. & Clin. Med. **9**:1 (Oct.) 1923.

The cause of death in superficial burns was made the subject of an experimental study by Robertson and Boyd. Skin, subcutaneous tissue and muscle burns were produced in anesthetized rabbits. Typical symptoms, with shock, followed the production of the burn in all cases. These facts emerge: Death from burning occurring within the first twenty-four hours is practically always due to primary shock; later than this, it is due to toxic shock. There is a toxin produced in burned tissue, in larger quantities in skin burn, which circulates in the blood, either in, or absorbed by, the red blood corpuscles, and which causes the symptoms seen in bad superficial burns, and in some cases death. Extracts of burned skin were found to be toxic. Extracts of skin burned postmortem were innocuous. The contents of burn blisters are not toxic. That there is increased protein catabolism in burns was evidenced by the increase in the nonprotein nitrogen and urea nitrogen of the blood. Whole citrated blood from burn cases is toxic. The blood serum is not toxic. Solutions of the corpuscles properly treated are more toxic than whole blood. The toxic substance consists of two portions, one of which is thermostabile, diffusible and neurotoxic; the other is thermolabile, colloidal and necrotoxic. Chemically, the toxin consists of primary and secondary proteoses. No evidence of the production of antibodies against the burn toxin could be found.

WARNING AGAINST USE OF ARSPHENAMIN IN TREATMENT OF SYPHILIS IN HEMOPHILIA. J. Rosenbloom, J. Lab. & Clin. Med. **9**:57 (Oct.) 1923.

A man consulted Rosenbloom for continual bleeding from a tooth socket following tooth extraction. His hemoglobin was 40 per cent.; red corpuscles 2,300,000, and Wassermann reaction 4 plus. Transfusion was done. The bleeding did not stop. Following the use of horse serum and transfusion, an injection of 0.6 gm. of arsphenamin was given. Within one hour following the injection all of his gums commenced bleeding at an alarming rate, the hemoglobin falling to 30 per cent. In spite of two more transfusions, the use of coagulose, horse serum, emetin, etc., the man continued to bleed, and two weeks following the injection of arsphenamin he died from anemia due to the hemorrhages.

TRANSIENT UNILATERAL HYPERHIDROSIS LOCALIS IMMEDIATELY FOLLOWING EATING OF HIGHLY ACID FOOD STUFFS. R. Hall, Irish J. M. Sc., October, 1923, p. 291.

Hall relates the case of a man who would have a reddish blush over his right cheek bone about midway between his eye and ear immediately after

eating highly acid food-stuffs such as rhubarb, stewed gooseberries, baking apples or vinegar (either hot or cold), and this was quickly followed by small beads of sweat over the blush spot, which then gradually resumed its normal appearance. Nothing was found in the general condition to account for this.

EFFECT OF RADIOACTIVE RADIATIONS AND ROENTGEN RAYS ON ENZYMES. II. EFFECT OF RADIATIONS FROM RADIUM EMANATION ON PEPSIN IN SOLUTION. R. G. Hussey and W. R. Thompson, J. Gen. Physiol. **6**:1 (Sept.) 1923.

Hussey and Thompson introduce a unit to express activity or power of a given preparation of radium emanation. They have named this unit the curie-power and defined it as the activity of 1 curie of radium emanation. They suggest the introduction of this unit in order that more comprehensive statements of experimental observation may be made.

EARLY ACUTE FORMS OF NEUROSYPHILIS. Nonne, Rev. méd. Uruguay **26**:350 (Aug.) 1923.

Nonne recalls that acute meningitis of syphilitic origin is rare, but he has encountered five cases. The extremely acute meningitis in one young woman developed four months after infection (from a kiss). The pressure in the spinal fluid was 500 mm., but under specific treatment it had returned to normal by the sixth week. The prognosis is generally favorable under specific treatment, but one of his patients in this group, a man aged 48, developed meningitis six months after infection for which he had been given mercury and sixteen injections of arsphenamin. Resumption of specific treatment failed to avert the fatal outcome, and the microscope revealed inflammation of the pia throughout the entire nervous system. In a fifth case the febrile meningitis developed four weeks after infection, but it apparently subsided under neo-arsphenamin treatment. Headache and convulsions returned two months later, and a third time after three months more. The spinal fluid responded to all the tests each time. Necropsy four weeks later revealed a gummatous meningo-encephalitis. The treatment apparently had been thorough in these two men; the three women recovered. Nonne's experience teaches that syphilis should always be considered in every case of acute cerebrospinal meningitis. There were no characteristic features in these cases; they seemed to be ordinary epidemic meningitis.

PHOTOTHERAPY IN DERMATOLOGY. Sicilia, Rev. med. cir. Habana **28**:535 (Aug. 10) 1923.

Sicilia defines the three main groups of skin and syphilitic disease which are peculiarly amenable to radiant energy and great heat; itching dermatoses or essential pruritus, affections with torpid secretion and vitality, especially with sluggish metabolism, but above all cases calling for absorption of effusions and suffusions.

TREATMENT OF ECZEMA IN INFANTS. P. Rueda, Semana méd. **2**:81 (July 19) 1923.

Rueda reports twenty-seven cases of seborrheic eczema in infants treated on the basis that the pancreas was responsible for the affection.

EARLY NEUROSYPHILIS. H. Pette, Med. Klin. **19**:1147 (Aug.) 1923.

Pette believes that the early syphilis of the central nervous system has become more frequent since the introduction of arsphenamin. All his patients, except three, had been treated with insufficient doses.

CATARRHAL AND SYPHILITIC JAUNDICE. E. Klopstock, Med. Klin. **19**:1156 (Aug.) 1923.

Klopstock finds that the speed of sedimentation of blood corpuscles is increased in syphilitic (and infectious) jaundice while it is decreased in simple catarrhal jaundice.

TUBERCULOSIS OF SKIN AS SYSTEMIC DISEASE. Wien. klin. Wchnschr. **36**:611 (Aug. 23) 1923.

Fischl confirms Löwenstein's theory: The skin acquires a predisposition to tuberculosis, if the first infection occurred in it. Tuberculosis of the skin is rarely associated with a progressive tuberculous affection of other organs.

SYPHILITIC PITUITARY CACHEXIA. V. Jedlicka, Casop. lek. cesk. **62**:1027 (Sept. 29) 1923.

Jedlicka describes a case of syphilis in an aged man. The secondary eruption spread over the greater part of the body and while it was still present gummas developed, about seven months after the onset of the secondary symptoms. The patient did not react to treatment and died from cachexia, which was apparently caused by a gumma in the pituitary gland. Eight photomicrographs illustrate the findings.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Oct. 4, 1923

PAUL E. BECHET, M.D., *Chairman*

LEPROSY (SEVEN CASES). Presented by DR. HOWARD FOX.

The patients were inmates of the Riverside Hospital, to which such cases had been sent from other city institutions and isolated prior to being transferred to the national leprosarium in Louisiana. Two other lepers in this colony refused to be presented. Of the seven who were present four were Chinese, two South Americans and one Greek. All of the cases were of the mixed type of leprosy, the manifestations of the disease being well marked in all except two. In these cases the diagnosis had been confirmed by histologic examination. All of the patients showed enlargement of the ulnar nerves, and all except one the characteristic swelling, pigmentation and wrinkling of the skin of the hands. There were no ocular manifestations except in one patient, who showed a slight unilateral conjunctivitis with some ciliary tenderness. In only one case were the nails involved. The Wassermann test (blood) was positive in one case, in which it seemed probable that there was a concomitant infection of syphilis. In three cases the Wassermann test was negative. All of the patients had received treatment with intramuscular injections of ethyl esters of chaulmoogra oil. Improvement was noted in all except one case; in two it was marked. In most of the cases the disease had appeared, according to the patients' statements, a year or two after their arrival in the United States. In one case the disease was said to have appeared after the patient had been in this country for over eleven years.

CASE 1.—A. B., aged 23, born in Columbia, South America, a clerk, had been in the United States for two years. The disease had appeared one year ago. At the present time he showed only a slight enlargement of the ulnar nerves and a dull reddish macular patch between the eyebrows. The sensations of touch, pain and temperature were normal in this lesion. He had previously presented other patches on the body, from one of which a piece of tissue had been excised at the City Hospital and a histologic diagnosis of leprosy made. The patient had received about twenty injections of ethyl esters in addition to chaulmoogra oil by mouth, and with the exception of the patch between the eyebrows, the eruption had entirely disappeared. The Wassermann test, which was said to have been frequently performed, was negative.

CASE 2.—S. C. S., aged 26, Chinese, a sailor, had been in the United States about fifteen months. The disease had first been noted six months ago. It was of mild type, consisting of macules and beginning nodules. There was marked atrophy of the last phalanx of the right thumb and dystrophic changes of two of the nails. He presented at one time a mild unilateral conjunctivitis with some ciliary tenderness, but a mobile pupil. There had been no improvement from treatment.

CASE 3.—P. N., aged 27, Greek, a cook, had been in the United States for twelve years. He claimed that the disease had not appeared until seven months ago. It affected the face, trunk and extremities, and was of severe nodular type. There had formerly been considerable ulceration, which had cleared up under antisyphilitic treatment, the Wassermann test changing from strongly to weakly positive. There was also a history of syphilis. The improvement in the eruption was marked, though it was difficult to say how much effect the treatment had had on the leprous lesions.

CASE 4.—C. N., aged 15, a Chinese school boy, had been in the United States for three years. The duration of the disease was said to be one year and was of a mild type. The Wassermann test was negative. There had been improvement under treatment.

CASE 5.—M. G., aged 44, Chinese, a fireman, had been in the United States for four years. The disease, which had appeared one year before, was of macular type affecting chiefly the face, arms, and thighs. One patch on the cheek suggested the appearance of a lupus erythematosus. On the thighs the lesions had a circinate figuration. He had improved under treatment.

CASE 6.—In H. F., aged 22, a Chinese laundryman, the disease had appeared three years before; it was of nodular type and of moderate severity, affecting the face, trunk and extremities. There were numerous brown macules on the trunk. Histologic examination was positive for leprosy. The Wassermann test was negative. He had improved under treatment.

CASE 7.—C. T., aged 25, Chinese, a cook had been in the United States for eight years; the eruption appeared six years before. It affected the face and extremities chiefly, and was of the nodular type and of moderate severity. The Wassermann test was negative. The patient had improved under treatment.

DISCUSSION

DR. CHARGIN said that about two years before he had presented before the Society a patient with case of macular anesthetic leprosy, whom he was treating with the ethyl esters of chaulmoogra oil. The patient had shown marked improvement, and if it continued one might expect an eventual cure.

DR. WOLF said the case of the Greek was the one of greatest interest, as he presented nodules on the tongue which were worthy of note because they were uncommon.

BOECK'S SARCOID. Presented by DR. ROSTENBERG.

Miss F., aged 19, an American, whose past and family history were irrelevant, had skin trouble that started two and one-half years before, when a small bluish red mark had appeared on the deltoid region of the left arm. This lesion had increased in size without causing any subjective symptoms. A year and a half later, another similar lesion appeared in close proximity to the first one, and about eight months ago one on the right side of the neck and scalp. The patient came under observation about six weeks before presentation. She appeared to be a healthy, robust looking young girl, and a physical examination revealed a normal condition of all her internal organs. A Pirquet test was positive, a Wassermann reaction negative.

On her upper left arm there were two irregularly shaped oval lesions, the larger one about 1 inch by ½ inch (2.54 by 1.27 cm.) in size. The periphery of the lesion consisted of a number of pinhead sized superficial reddish nodules;

the center was smooth and of a somewhat livid tinge. The lesion next to it looked about the same, except that the periphery was not so much infiltrated. The lesion on the neck looked as if it had involuted to some extent, the skin appearing wrinkled and atrophic.

The patient had been treated with injections of sodium cacodylate and the roentgen ray, and all the lesions had improved markedly.

DISCUSSION

DR. POLLITZER said that the lesions in this case showed scarcely any infiltration. He understood that this was the result of treatment, and that the lesions seemed to be undergoing involution.

DR. BECHET said he had seen the patient several times before she was seen by Dr. Rostenberg. The lesions were then of a boardlike induration and typical of Boeck's sarcoid. The lesions had greatly improved.

SARCOID. Presented by DR. SCHEER.

B. S., aged 60, married, born in Russia, came to the Mount Sinai Clinic for an eruption which had been present about three months. The lesions were located on the upper part of the back, shoulders and upper part of the arms. They were most numerous and largest over the left scapular region, less numerous on the right scapular region, still less numerous on the shoulders, and fewest on the upper arms. There was one small lesion above the left breast. The largest lesion was oval in shape and about one and a half inches (3.81 cm.) in diameter, and it had a few smaller lesions around it. The smaller ones varied in size from that of a pinhead to that of a split pea. They were all firm, infiltrated and of a lilac color. There was no pain or tenderness. A slight itching was present only at the outset.

DISCUSSION

DR. LEVIN said that he had seen a group of cases in which the lesions occurred on the extremities and resembled sarcoid clinically. These, however, on microscopic examination were found to be neurofibromas. They were made up of whorls of connective tissue fibers and cells, and were especially rich in cellular content. In the case that was presented by Dr. Scheer, the lesions, particularly the one on the left arm, were suggestive of this type of lesion. He favored the diagnosis of neurofibroma. He did not use this term as synonymous with Recklinghausen's disease, but referred to skin lesions with a definite pathology.

DR. SCHEER said he had not seen any neurofibromas that resembled sarcoid, and he thought that this was as typical a case of sarcoid as could be found. A biopsy had been made only a few days before, and a report would be made at the next meeting.

DARIER'S DISEASE. Presented by DR. THORNLEY.

F. F., a woman, aged 21, born in Russia, whose family and previous history were negative, had a condition that began eight years before, when several papules appeared on her chin. There were no subjective symptoms. The condition gradually increased in extent, but always improved during the colder months.

DISCUSSION

DR. BEEGEL said that the patient had come to the hospital two weeks previously. The lesions on the face were not so typical as those in other places, where there were typical verrucous lesions. She had had the condition for eight years, the lesions first appearing on the chin. Before coming to the hospital she had received some roentgen-ray treatment, but as an erythema developed afterward she became frightened and ceased treatment. After coming to the hospital she was given roentgen-ray treatment in fractional doses, but was again complaining of swelling of the face.

DR. ABRAMOWITZ said that he first made a diagnosis of seborrheic dermatitis, but promptly changed it to Darier's disease on noting the keratotic follicular lesions behind the ears and on the backs of the hands. The history was that she had been treated by Dr. Bechet for some time, first as having a case of seborrheic dermatitis, and afterwards as having Darier's disease. The history of the disappearance of some of the lesions might be accounted for by considering that the patient had seborrheic dermatitis combined with Darier's disease, the seborrheic dermatitis occasionally improving.

DR. BECHET said he had observed the patient at the University and Bellevue Clinic for two or three years, and had presented her about two years previously with the diagnosis of Darier's disease. At that time no one seemed to agree with the diagnosis, considering it more probably seborrheic dermatitis. In spite of this he had adhered to his original opinion, and he was glad to see that on the second presentation this opinion was unanimously verified.

GRANULOMA ANNULARE. Presented by DR. ABRAMOWITZ.

T. W., a school girl, aged 10, of Jewish parentage, had an eruption confined to the fingers that had been present for one year. On the backs of the index and ring fingers of the left hand were two one-quarter inch (6.35 mm.) circular lesions, with erythematous warty edges and centers. On the knuckles of the right index finger and on the first joint of the right thumb were two similar lesions of the same size. The inner side of the right middle finger presented the largest lesion, about one inch (2.54 cm.) in size, with polycyclic edges. No histologic study was made, as it was a classical case of this disease.

GRANULOMA ANNULARE. Presented by DR. ROSEN.

H. M., a girl, aged 2½, was born in New York City, and was an only child. The mother had had no miscarriages, and was perfectly well. The child had had an attack of measles six months previous to the appearance of the skin disease. She looked well nourished, and was normal in weight and development for her age. Examination revealed about ten lesions, varying in size from that of a ten cent piece to that of a twenty-five cent piece, located on the forearms, thighs and lower extremities. These were annular in outline with an infiltrated rim. Within the circle the skin appeared to be of normal color and texture. The infiltrated area was slightly red. There were no changes visible in the skin immediately surrounding each lesion. Palpation gave a better idea as to the nature of the affection than did inspection. There was no evidence of atrophy or scarring in any of the lesions. A Wassermann test was taken, but the result has not been reported yet.

DISCUSSION

Dr. Pollitzer said that the case of the little girl presented by Dr. Abramowitz showed all the typical features of granuloma annulare. As to the younger child, he did not feel that the youth of the patient militated strongly against the diagnosis. There was not much difference between a child of 2½ and one of 8½ years. On the other hand, as Dr. Rosen had said, the lesions were not entirely typical. He was inclined to support the diagnosis of a granuloma annulare by exclusion, although the lesions were larger than was usual. It was difficult to reach a conclusion about them; in a way they were characteristic —a sharply defined, annular dark red infiltration and clear center; but he would wish to put a question mark after that diagnosis.

Dr. Rostenberg said he had hoped to show a case which he had observed in the Spring. It was a typical case, and he had written to the patient to come, but when seen yesterday the lesions had disappeared entirely. He had been under the impression that these cases were refractory to treatment, but this one had cleared up spontaneously.

Dr. Wolf suggested a diagnosis of early morphea. In a superficial examination, he had noted a uniform infiltration with a pinkish border. The lesions were round in contour with no tendency to papular formation, which led him to think it was not granuloma annulare, although he might be mistaken.

Dr. Abramowitz said that Dr. Rosen's patient presented an eruption of a different type of granuloma annulare, more like Crocker's erythema elevatum diutinum.

A CASE FOR DIAGNOSIS. Presented by Dr. Thornley.

M. A., a boy, aged 9, born in the United States, was well until a year ago. His parents, three brothers, and one sister were all well. Another sister was being treated in the tuberculosis clinic for suspicious signs in the chest, which were clearing up. A year ago the patient began to cough; he came to the clinic, where suspicious signs were found in his chest. These signs had practically disappeared. Ten months ago, an eruption appeared over the sternum, which in spite of treatment at various institutions became worse. The lesion consisted of a small follicular, papular eruption situated over the trunk and arms in groups. The larger groups were at the base of the neck, over the sternum, the upper part of back, and around the umbilicus. Smaller groups were over the anterior surfaces of the elbows. The eruption appeared to be very itchy.

DISCUSSION

Dr. Pollitzer suggested that the diagnosis lay between lichen scrofulosus and prurigo. Against prurigo was the distribution and—although many of the lesions were scratched—the absence of the intense itching characteristic of that disease. The lesions themselves and the groupings were sufficiently characteristic of lichen scrofulosus, and he favored that diagnosis.

Dr. Highman agreed with Dr. Pollitzer that the diagnosis lay between lichen scrofulosus and prurigo, only he would invert the probabilities. The lesions were small papules, more or less scratched, and many were on the extensor rather than on the flexor surfaces. Some seemed to be of a type suggesting neurodermite. The second consideration was lichen scrofulosorum, but the lesions had not the characteristic grouping of that condition on the torso. It was impossible to reach a diagnosis through argument; the microscope would soon settle the matter.

Dr. Howard Fox said he did not understand how a diagnosis of lichen scrofulosorum could be considered in this case. This disease, according to his conception, was one that did not itch. In the present case there was no question about the presence of more or less severe scratching. The patches represented an inflammatory itchy disease, that in his opinion might be classed as a prurigo-like eruption, eczema, or the papular type of Duhring's disease. It certainly did not have the distribution of ordinary prurigo.

Dr. Chargin agreed with Dr. Highman and with Dr. Fox that it was not a case of lichen scrofulosus. In lichen scrofulosus the lesions while grouped were small, follicular, reddish brown, and were usually seen on the sides of the body and on the lower lumbar region. In this case the lesions were papular, located on a somewhat infiltrated skin, and there was marked itching, which was proved by the large number of scratched off papules. In his opinion, this case should be classed in the neurodermite group.

Dr. Wise said he favored the diagnosis of prurigo.

Dr. Levin said that only two conditions were to be considered: lichen scrofulosus and neurodermite. The only points that might suggest the first were the doubtful history of suspicious tuberculosis and the follicular character of some of the papules. Nothing else suggested lichen scrofulosus. The boy was underdeveloped, small in stature, underweight, not alert, and had a dry skin with a tendency to scaling. The eruption occurred in the usual sites for neurodermite, was pruritic, the papules were excoriated, and there was some lichenification. In his opinion, the case was that of a generalized neurodermite.

Dr. Thornley said that at first glance the case seemed to be lichen scrofulosus, but closer examination showed the scratched and excoriated papules, and they were not so certain. There were some glistening white lesions that even suggested lichen planus.

A CASE FOR DIAGNOSIS. Presented by Dr. Rostenberg.

P. H., aged 63, an artist, had a condition that started after a slight accident whereby he struck his forehead on a piece of furniture. There was no bleeding at the time, but a few days afterward a small red spot, about the size of a five cent piece, appeared, which gradually increased in size and grew to its present shape in about three to four months, remaining stationary after that. His previous history was irrelevant. On inspection, there was found over the center in the frontal region of the scalp an irregular, oval lesion about 2 by 3 inches (5.08 cm. by 7.62 cm.) in diameter, abruptly merging into the normal surrounding skin. It was bright red. There was no scaling, but a slight degree of atrophy. On closer inspection, a large number of somewhat darker red punctae were seen throughout the lesion, some the size of a dot, others as large as a pinhead, giving a somewhat mosaic-like appearance. There were no subjective symptoms, with the exception of a slightly tense feeling over the lesion; there was no itching.

DISCUSSION

Dr. Scheer said he thought that the rather sharp, straight outline of the lesion and jagged appearance on the left border suggested a dermatitis artefacta.

Dr. Howard Fox said that in his case of lymphogranuloma there were elevated tumors, the color of which was somewhat similar to that of the lesion presented by Dr. Rostenberg's patient. He would not hazard a diagnosis in this case.

DR. ROSTENBERG said he had hoped to get some information concerning the case. He had excluded any factitious dermatitis; the man was not neurotic, and was very desirous of getting rid of the condition. He had been referred a few months ago with a history of having met with an accident, after which this condition developed and remained stationary. There was a slight atrophy of the lesions, and Dr. Rostenberg said he though it might be an atypical lupus erythematosus, but he would not venture a positive diagnosis of that condition. The condition had not changed during the last six months.

MACULAR ATROPHY. Presented by DR. ROSTENBERG.

L. C., a man, aged 29, American born, dated his present condition back to an itchy skin eruption which he had had last April, for which he had used phenolated petrolatum.

He came to the clinic last July, at which time he had a typical ulcus durum. He denied having had any syphilitic infection before. When he undressed, his present skin trouble was found. He presented an innumerable number of discrete, more or less prominent lesions, of pinhead to small pea size, of normal skin color, the surface being relaxed and shriveled but becoming normal when put on a stretch. The lesions became more prominent the longer the skin was exposed. The interesting feature of this case was the fact that while the lesion corresponded to the macular type of atrophy due to syphilis, this atrophy started before the patient had developed syphilis.

DISCUSSION

DR. WISE said that most of the cases of macular atrophy occurred at the site of preexisting lesions, but he did not think that was the case in this instance.

DR. ROSTENBERG said it was a case of macular atrophy independent of syphilis, although the patient did have syphilis. The man came to the clinic with a primary lesion when the atrophy was also noticed.

A CASE FOR DIAGNOSIS. ANGIOMA SERPIGINOSUM? Presented by DR. BECHET.

W. H., a man, aged 49, born in the United States, said that the lesion had begun on the back of the neck two years previously, first appearing as a patch about half an inch (1.27 cm.) in diameter beneath the right ear. It gradually increased in size, covering the entire cervical region from ear to ear. A smaller patch appeared on the right temple. The lesions consisted of a network of dilated capillaries, in annular formation with normal skin between; on stretching the skin this arrangement closely resembled a fine meshed fish-net. The border of the lesion on the temple had a serpiginous outline. The papules and cayenne pepper points of true angioma serpiginosum were absent. The mesh work of delicate vascular rings was of a reddish yellow color. There was no history of any prolonged exposure to the actinic rays.

DISCUSSION

DR. LANE said he did not see anything that suggested angioma serpiginosum.

DR. WISE said he thought the man had chloasma, which was quite common on the side of the neck, and also had telangiectasia, which was also common on that part of the neck. He saw no resemblance to angioma serpiginosum.

DR. BECHET said that against the diagnosis of angioma serpiginosum were the absence of the bright red, purplish, pinhead sized papules, the cayenne pepper grains and marked serpiginous configuration. The border of the lesion on the temple, however, was noticeably serpiginous in outline, and the mesh-like, annular vascular rings, with the absence of a history of unusual actinic exposure, would at least suggest the possibility of angioma serpiginosum.

BLASTOMYCOSIS. Presented by DR. CHARGIN.

J. M., a man, aged 43, married, a cable splicer, in 1919 suffered from active pulmonary tuberculosus, the sputum being positive for tubercle bacilli. He received sanatorium treatment until 1921, at which time he was discharged as having an arrested case. In March, 1923, he had a pulmonary hemorrhage which kept him in bed for about two weeks. During this period he received codein sulphate ¼ grain (0.016 gm.) three times a day. No other medication was administered at that time. Since then he had suffered from a "cold" on one or two occasions, for which he had taken home remedies. Careful inquiry revealed that the patient had taken no other drugs during the past seven months at least. He had had a slight cough during the early part of 1923, and the sputum, which was scant, was examined on six different occasions, always with a negative result. There had been no cough during the last six months. The patient said he did not have syphilis, and the Wassermann test proved negative.

The skin trouble began about five months before presentation, with a "pimple" on the forehead above the left eye. Of this there was at present merely a scar. This lesion healed spontaneously, as did also a lesion on the right wing of the nose, which appeared later. In the course of the following two months the rest of the lesions which the patient presented made their appearance. The eruption was limited to the face, and except for a single patch on the left wing of the nose, all were of the same general character. The lesion on the nasal wing, perhaps the last to appear, was irregular in outline, quite superficial, and was covered with a thin crust. The rest of the lesions that the patient presented may be described as follows: On the forehead, over its center about an inch above the root of the nose, was a five cent piece sized, round, raised and quickly crusted lesion. On the upper third of the bridge of the nose, extending to both sides, there was a bandlike lesion about ½ inch in width, and similar in all respects to the foregoing, except that the crust was heavier. The left side of the nose and adjacent cheek presented a semicircular patch with a polycyclic border. On the left cheek in the hairy region, in front of and below the ear, was the largest and most marked patch which the patient exhibited. This was circular, about the size of a half-dollar, and covered with a thick crust. On the border of several of the lesions very small pustules might be discerned. The crust covered affected area was uneven on the surface, either brownish or yellowish in color, and was evidently made up of ruptured pustules and blood. The upper part of the crust was quite friable so that when touched it crumbled; the deeper portion, however, was closely adherent to the underlying tissue, so that when removed bleeding was produced. The ulcers were definitely papillomatous, slightly raised, even with or slightly depressed below the level of the normal skin. The tissue was soft to the touch. There was no infiltration around the affected areas. No lymphangitis was present. The neighboring glands were not enlarged. The mucous membrane of the mouth was not affected. The temperature was normal. Subjectively there was no pain and no itching, and the patient's general condition was good.

Smears made from the discharge obtained from the depth of the ulcerated areas showed blastomycetes. A single culture proved negative.

DISCUSSION

DR. HOWARD FOX asked whether syphilis and bromoderma could be excluded.

DR. CHARGIN replied that the patient said he did not have syphilis, and the Wassermann test was negative. The question of the ingestion of bromids was carefully inquired into and could be ruled out. The patient gave a history of having taken codein sulphate for two weeks seven months before, but so far as could be learned he had not taken bromids. So far as a syphilitic lesion was concerned, there was not the slightest suggestion of ulcerating gumma when the crusts were removed.

CONGENITAL SYPHILIS WITH RECENTLY ACQUIRED SYPHILIS.

Presented by DR. PAROUNAGIAN.

S. F. H., a man, aged 25, single, an American, a cook, whose mother died in childbirth and whose father was said to have died of syphilis, said that at the age of 8 he had had ulcers on his legs which lasted for years, and the scars from which still remained. In 1917, he was in the United States Navy when one of the ulcers on his leg broke out. The naval surgeon diagnosed it as syphilis, and administered one dose of arsphenamin; this was followed by left-sided hemiplegia of two months' duration. The patient was placed in the hospital. When the Wassermann test was found to be four plus, treatment was continued with arsphenamin and mercury. Prior to leaving the hospital the Wassermann test was said to be negative.

His last exposure occurred about the middle of February, 1923; there was no evidence of a new infection until about the middle of August, 1923, when a generalized eruption, mucous patches in the mouth and throat, condylomata lata in the anal region and moist papules about the genitals appeared.

The patient reported at Bellevue Hospital on Aug. 21, 1923, with a four plus Wassermann test, a generalized papular eruption, palmar and plantar syphiloderms, mucous patches in the mouth and on the lips, and condylomata lata about the anus, with marked pigmented scars on both legs and an ulcer at the external malleolus. Under six neo-arsphenamin and three mercury salicylate injections, most of the lesions healed.

DISCUSSION

DR. WISE said that cases had been reported of persons with congenital syphilis acquiring syphilis in adult life. It was not proved, however, that this patient had a case of congenital syphilis, only a possible one. One would like to see the stigmas of congenital syphilis, such as Hutchinson's teeth, keratitis, and so forth. What Dr. Parounagian had to prove was that the patient had congenital syphilis; there was no doubt about his having acquired syphilis.

DR. POLLITZER said that these cases were interesting on account of their great rarity, and the question should be studied thoroughly before putting this on record as a case of congenital syphilis with late acquired syphilis. The conditions pointed strongly to syphilis in this patient when he was 8—the history of ulcerations which had left fairly characteristic pigmented scars, the history of a period in a good hospital where a diagnosis of syphilis had been

made and a positive Wassermann test established, the lesions clearing up and later followed by a negative Wassermann test—all this was good evidence of the patient's having had syphilis six or eight years ago. That the patient had a recent syphilis the group of symptoms detailed proved fairly satisfactorily. There was, however, only a degree of probability in all this, for neither Dr. Parounagian nor any other physician saw the primary lesion and the evidence that was characteristic of acquired syphilis. If that could be established or even if it were proved beyond question that this patient did have syphilis as a child, a satisfactory case of acquired syphilis in a person with congenital syphilis could be made out. It depended very much on the nature of the evidence of the previous syphilis, which Dr. Parounagian presumably had established to his satisfaction from the hospital records.

Dr. Parounagian submitted photographs showing deep pigmented scars of the lesions which the patient had had in early childhood, and also the palmar and plantar lesions, including the generalized eruption of his recent infection.

As a proof of congenital infection, in addition to the extensive pigmented scars on the extremities, the patient presented imperfect hair lines, and an extratubercle on his first molars—"tubercle of Mibelli." His incisors also bore witness to his congenital infection, and he had been told that his father had died of syphilis. While he was in the service, he had been treated in a naval hospital with injections of arsphenamin and mercury; according to his own statement, when he was discharged from the hospital the Wassermann reaction was negative, and the ulceration on his extremities had healed under the treatment. His last exposure had occurred in February, 1923, and during the summer of 1923 he had developed a generalized maculopapular eruption, mucous patches in the mouth and throat, condylomas about the anal regions, syphilitic alopecia, palmar and plantar syphilids, and a four plus Wassermann test.

Dr. Pollitzer agreed with what Dr. Parounagian had said, but he wished to know whether he had verified the statements of the patient concerning the diagnosis and treatment in a hospital.

Dr. Parounagian said he would try to ascertain all facts as far as possible.

Dr. Pollitzer said that it was important that the man's statements should be verified.

TINEA CAPITIS IN AN ADULT. Presented by Dr. Scheer.

M. B., a colored woman, aged 26, married, born in the United States, came to the Vanderbilt Clinic for treatment of a lesion on the scalp, which she said had been present for five weeks. From its appearance the lesion was probably at least twice as old. In the occipital region of the scalp there was a patch the size of a silver dollar, round, with numerous hairs broken off near the surface, and grayish scales. A microscopic examination of hairs showed ringworm of the microsporon variety.

DISCUSSION

Dr. Howard Fox said that this case was one of great rarity. While tinea was occasionally seen in the scalps of adults, he did not recall ever having seen such a typical patch of microsporon infection in an adult. The late Dr. Jackson, an authority on diseases of the scalp, had once told him that he had seen only one such case.

Dr. Rulison told of a case he had just seen in a girl aged 16, and asked at what age the condition became rare—after early or late puberty?

Dr. Parounagian said that several years before he had presented a man, aged 30, with a typical case of tinea tonsurans. The diagnosis was confirmed by microscopic and other examinations.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN). Presented by Dr. Scheer.

H. M., a boy, aged 8, had had the eruption for about eight months. He had been given phenolax at irregular intervals for the past year. The eruption was situated on the eyelids of both eyes, mainly on the upper lids. It consisted of sharply defined, pigmented patches of a slate gray color, occupying the entire surface of the lids. The mother said that at times the eruption became quite red, but she could not recall the association of flare-up with the administration of phenolax. On being informed of the nature of the eruption, she refused to permit further administration of the drug.

DISCUSSION

Dr. McCafferty told of a case with pigmentation of the lesions of the mucous membrane. The patient was treated with high colonic irrigations, and the lesions cleared up in two or three weeks.

Dr. Highman said he had seen lesions of this kind resulting from the use of antipyrin, but this was the first time that he had seen this type of lesion resulting from ingestion of phenolphthalein.

LARVA MIGRANS. Presented by Dr. Scheer.

H. B., a girl, aged 6½, came to the Vanderbilt Clinic with an eruption of two years' duration situated on the right leg. She had been in New York four weeks, previously to that in Florida for two months, and before that in Texas, which was her home. The eruption started on the inner side of the right foot, near the arch. It went around the heel to the other side, then back to the starting point, and then began moving up the leg. The eruption had spread about 3 inches (7.62 cm.) during the past three days. It consisted of a red streak with an inflammatory area about one-half inch in diameter at the point of spreading.

PARAPSORIASIS. Presented by Dr. Chargin.

M. A., a man, aged 39, married and the father of three children, said that he had had syphilis since 1914, for which he had been treated at intervals with arsphenamin and mercury. His present eruption appeared a year ago, and had persisted despite treatment with various local remedies. During this year he had also received about ten injections of arsphenamin and perhaps twenty or more injections of mercuric salicylate, without the slightest effect on the present eruption. The eruption covered the entire body except the face and scalp. It was most marked on the trunk, and the lesions were small, papular and macular in character. Scaling was very much in evidence, although it was small in character, and was seen mostly at the border of the individual lesions. The color was brownish. There were no lesions of the en plaque variety. There were no subjective symptoms.

PERSISTENT PIGMENTARY SYPHILIS. Presented by DR. PAROUNAGIAN.

E. J., a woman, aged 20, unmarried, born in the United States, a packer, reported at Bellevue Clinic on July 12, 1923, with the remains of a chancre about the vulva, pigmentary syphiloderm, alopecia syphilitica, condylomata lata about the anal regions and a four plus Wassermann test. Since admission she had received eight neo-arsphenamin and seven mercuric salicylate injections. While most of the active lesions had disappeared, the marked pigmentation persisted. Silver arsphenamin was not employed in this instance so that the pigmentation could not be charged to that drug.

SECONDARY SYPHILIS, WITH MARKED PIGMENTATION ABOUT THE CHIN AND FOREHEAD. Presented by DR. PAROUNAGIAN.

T. McM., aged 23, a native of the Philippine Islands, reported at Bellevue Clinic on Sept. 24, 1923, with marked roseola, general adenopathy, and a four plus Wassermann test. No evidences of chancre could be detected. He was given one injection of neo-arsphenamin; while the roseola mostly subsided, the peculiar pigmentation about the mouth and forehead was striking.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. PAROUNAGIAN.

L. M., aged 52, single, an American laborer, whose past history was negative, said he had not had any venereal trouble. The Wassermann reaction on Sept. 17, 1923, was negative. He had had no trouble until about seven months ago, when he had a fine warty eruption on the left hand, in the web between the little and ring fingers. He complained of "needle-like" pain on flexing the fingers. The eruption had persisted.

On the palmar surface of the little finger of the right had, over the proximal phalax, there was an indurated, warty eruption, which was also in the web between the little and ring fingers, extending up on the dorsum of the hand three fourths of an inch, where there were several large red areas from 2 to 10 mm. in diameter.

The diagnosis was clinical; no biopsy had been made or treatment instituted.

LPUS ERYTHEMATOSUS OF THE FACE, SCALP, LIPS AND BUCCAL MUCOSAE. Presented by DR. PAROUNAGIAN.

A. S., a man, aged 43, Italian, married, a lithographer, said he had had the condition for thirteen years. It appeared first on the face, and later on the scalp, lips, etc. The patient had had various forms of treatment at different clinics. His family history was negative as to tuberculosis or skin affections of similar character. The Wassermann test proved negative, and no evidences of syphilis could be detected. There was no question in regard to the diagnosis of lupus erythematosus; the patient was presented simply on account of the marked involvement of the mucous membranes of the mouth and lips.

EROSION OF GLANS PENIS. Presented by DR. THORNLEY.

OSCAR L. LEVIN, Secretary.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 17, 1923.

EDWARD A. OLIVER, M.D., *Presiding*

FIXED EXANTHEM. Presented by DRS. ORMSBY and MITCHELL.

A man, aged 32 years, who had had a generalized recurrent eruption in the same areas for the past five years, had had about ten attacks in all. Usually one attack occurred in the summer and one in the winter. A given attack lasted from five to six weeks. The erythema then subsided and the lesions persisted as brownish macules. The patient took Epsom salts as a cathartic, but he had never taken phenolphthalein in any form. There was a history of chancre two years before the onset of the eruption.

The patient was first seen on Aug. 15, 1923, at which time a photograph had been made. At the time of presentation the patient was recovering from an acute attack, the second since coming under observation in August. A comparison with the photograph made at that time revealed that the lesions were identical in size and distribution.

DISCUSSION

DR. STILLIANS said he believed it was a fixed eruption of unknown origin. He had presented a case some months before, in which no history of medication or use of phenolphthalein could be elicited.

DR. SENEAR said he had seen the patient at the clinic and had had the same impression as to diagnosis. He had been unable to obtain any history of the use of drugs. Dr. Weber had seen the patient at a later date at the dispensary, and at that time he had said that he had taken some pills. Dr. Senear said it was possible that the history was unreliable.

DR. ORMSBY said that not infrequently these eruptions were due to phenolphthalein, and that it was impossible at times to obtain a positive history of drug taking from the patients. Two years before they had had a patient who had denied taking any laxative drugs. Dr. Mitchell also cross-examined the patient carefully, without result. Later the patient volunteered the statement that he had occasionally taken phenolax. This showed that patients at times fail to remember that they have taken laxative drugs. At present there was a patient coming to the office for treatment for angioneurotic edema, who incidentally had a group of three lesions of the fixed exanthem type. This patient was the wife of a physician, and both the physician and the patient were sure phenolphthalein had not been used. Dr. Ormsby said that it might be possible that lesions of this type might be produced by other than the two or three drugs now positively known to be responsible for the major portion of such exanthems.

DR. MITCHELL said he had talked with this man repeatedly concerning the taking of drugs. The patient was intelligent and every way had been tried to trap him. He admitted that he took Epsom salts, but was absolutely sure that he had never taken anything else. He had repeated positively that he had taken no pills. Some of the lesions had had large bullae which were not, as a rule, found in the ordinary fixed exanthem. It might perhaps be one of the type of recurrent erythema multiforme cases which occurred always in the same areas and which had been described by MacKee.

NOTE.—Since the foregoing presentation, Dr. Mitchell has given the patient a 1 grain dose of phenolphthalein, and later a 2 grain dose, and on neither occasion was there any lighting up of the exanthem.

KERATOSIS. Presented by DR. RAVITCH.

A man, aged 55, had extensive keratosis of the feet and hands, and some keratotic places were disseminated on the arms and legs. The attack followed a dozen intravenous arsenical injections and was severe, affecting the mouth and tongue, causing a bad case of glossitis with numerous fissures and leukoplakic areas. The toes, fingers and tongue had become numb. The patient had been given six intravenous injections of sodium hyposulphite, which had improved his keratosis, but at the time of presentation there were some elevated red plaques. The patient was being given calcium chlorid therapy.

DISCUSSION

DR. STILLIANS said he thought it was a case of lichen planus.

DR. SENEAR and DR. LIEBERTHAL agreed with that diagnosis.

DR. ZEISLER said that although somebody had suggested a lichen planus-like eruption following arsphenamin, it should be called straight lichen planus. He was certain that the lesions were typical of lichen planus.

DR. RAVITCH said that these lesions would clear up and then recur. The patient had been examined by a neurologist who had given him fourteen injections of arsphenamin. He was not convinced that it was a case of lichen planus. It did not follow that the patient was suffering from lichen planus because some of the lesions had undergone lichenification.

A CASE FOR DIAGNOSIS. Presented by DR. LIEBERTHAL.

A woman, aged 42 years, who had a bean-sized lesion on the right side of the bridge of the nose near the inner canthus, for nearly a year had noticed a yellow spot where the present lesion had developed nine months before. At the first examination it showed an elevated, scaly periphery with a slightly depressed center.

DISCUSSION

DR. ORMSBY said that lupus erythematosus was the most probable condition that might induce such a lesion.

DR. SENEAR said he thought the outline of the lesion, which was not crusted but scaling, was suggestive of lupus erythematosus, but like Dr. Ormsby he was not positive. He thought there were other possibilities, particularly epithelioma.

DR. LIEBERTHAL said that when he first saw the case lupus erythematosus had been his tentative diagnosis, but the second time he had seen the patient there were nodular formations on the upper border which did not exactly fit into the picture. Local applications were made, which produced irritation, and therefore the crust had formed.

A CASE OF SCLERODERMA. Presented by DR. LIEBERTHAL.

A woman, aged 42 years, had developed lesions on the extremities during the past two years. They consisted of roundish flat plaques. The oldest lesions were situated over both large toes nearly symmetrically, and extended from the proximal phalanges over the dorsum of each foot about one inch and a half (3.8 cm.). Their transverse diameter measured about three quarters of an inch (19 mm.) each. These lesions showed in their proximal and medial parts (about a fifth of the whole lesions) firm infiltration and elevation, and pink

coloration, while the rest was of normal consistence, yellowish and pink. There were over the prolongation of the proximal phalanx of the middle toe of the right foot a bean-sized plaque; above the right internal malleolus one of the size of a quarter; one of half dollar size over the right calf and a small bean-sized lesion on the ulnar side and the middle of the right forearm. All of the last four lesions were bluish red and of firm consistency throughout, flatly elevated, with more or less depression, and yellowish in their central parts. Slight desquamation was present on all the lesions. At no time had there been any subjective symptom. The blood Wassermann test was negative, and the patient was otherwise in good physical condition. Microscopic specimens supplemented the demonstration.

DISCUSSION

DR. MOOK said he thought that clinically the individual lesions looked like epithelioma, the kind of migrating epitheliomas with cicatrizing centers that were occasionally seen, but the histology, the increased masses of fibrous tissue and the lack of change in the epithelial structure of course ruled out epithelioma. Microscopically the epidermis was not thin, as was usual with as much fibrous tissue as this. Dr. Lieberthal, he believed, had presented it as a case of scleroderma, but Dr. Mook thought it was an unusual type of scleroderma.

DR. ORMSBY said that clinically the lesions appeared to be epitheliomas, but he thought the location was unusual. He had never seen scleroderma presenting lesions of this character. He also thought that granuloma annulare should be considered.

DR. SENEAR said he felt the same way about the lesions clinically, and was inclined to believe that they were epitheliomas.

DR. MITCHELL agreed.

DR. LIEBERTHAL said that on looking at the patient for the first time he took into consideration all the affections which Dr. Ormsby had mentioned. However, the deciding factor for his clinical diagnosis had been the changes above the large toe, which clearly indicated that spontaneous healing was taking place. On the other hand, the subsequent examination of the microscopic specimens, revealing a short atrophied horny layer, dense and sclerosed collagenous tissue throughout the corium with hyalin degeneration, strengthened his opinion.

EXFOLIATIVE DERMATITIS DUE TO ARSPHENAMIN. Presented by DR. WAUGH.

A man, aged 59 years, had been given five intravenous injections of arsphenamin at three or four day intervals. Three weeks later another series of injections was begun, and these had been given twice weekly, eight or ten in all being given. The last injection had been given on October 1, seventeen days before presentation. The day following this injection the patient had complained of intense itching over the surface of the body, and this had been accompanied by considerable erythema and edema. About one week later exfoliation had begun. At the time of presentation the patient was receiving sodium thiosulphate injections.

PARAPSORIASIS (LICHENOID TYPE). Presented by DRS. ORMSBY and MITCHELL.

A man, aged 25 years, had had an eruption on the arms and about the borders of the axillae for about four months. There was no sensation. Before coming

under observation several Wassermann tests had been made and one provocative injection given, all of which gave negative results.

The eruption was symmetrical and consisted of slightly scaling macules in retiform arrangement on the arms and in the region of the axillae, extending backward over the scapula and forward to the nipple line. Here and there was a papulomacule with brownish pigment suggesting urticaria pigmentosa. There was no urtication.

DISCUSSION

Dr. Mook said he thought of pityriasis rosea and parapsoriasis, but he was inclined to believe that a great deal depended upon the future course of the case. He thought it looked a little more like parapsoriasis than pityriasis rosea.

Dr. Zeisler and Dr. Stillians agreed with Dr. Mook.

Dr. Senear said the condition looked a little more like parapsoriasis.

Dr. Mitchell said that the fact that most of the lesions were on the arms and thighs and not on the trunk was decidedly against pityriasis rosea. There were some slightly papular lesions which were more of a lichenoid type of parakeratosis. He thought it was a case of parakeratosis variegata or lichenoides.

A CASE FOR DIAGNOSIS. Presented by Dr. Senear.

A negro, aged 53 years, fifteen years previously had had a lesion on the penis which had been associated with swelling in the left inguinal region. This had been operated on about a year and a half later, with curettage of the part affected. It had healed, but since that time there had been a steady progression toward the pubic region, with the formation of swellings which broke down and discharged pus.

DISCUSSION

Dr. Lieberthal said he thought the condition was inguinal granuloma.

Dr. Mitchell agreed.

Dr. Stillians said that the fact that there was so much pus made him doubt the diagnosis of granuloma inguinale.

Dr. Senear said that he recalled that last year Randell, after Symmer had shown two cases, began a search for this condition. In a series of sixteen patients that came in after that they found fifteen who had definite granuloma inguinale. In this particular case Dr. Senear had thought it a chancroidal lesion rather than granuloma inguinale, although the progress had been more like that of the latter. There had been a ready response of the indurated mass to the milk preparation given.

PITYRIASIS RUBRA PILARIS. Presented by Dr. Stillians.

A boy, aged 5, had had "chapped skin" on the legs, feet, forearms, hands, ears, cheeks and buttocks since he was eight months old. This condition always grew worse during cold weather but did not heal entirely during the summer. His paternal grandfather, father and father's sister had similar lesions on the backs of the hands. The skin, with the exception of that on the cheeks, which was bright red and fissured, was thickened and dry. On the extremities the follicles were marked by black points, which were striking on the backs of the

proximal and middle phalanges, the backs of the hands and the extensor surface of the forearms. The palms were thick and inelastic, with smooth hyperkeratoses. The child was apparently in good health, and the basal metabolism rate had been + 16 at the beginning of the period and — 15 at the end.

DISCUSSION

DR. MCEWEN said he believed this was a case of pityriasis rubra pilaris.

DR. MOOK agreed with that diagnosis.

LUPUS ERYTHEMATOSUS. Presented by DR. WAUGH.

A man, aged 24 years, had a disorder that had been present for five months. There were a number of split pea to dime-sized lesions on the nose, cheeks and lobes of the ears. Some of the lesions showed atrophic scarring in the center.

A CASE FOR DIAGNOSIS. Presented by DRS. ORMSBY and MITCHELL.

A negress, aged 48 years, had a generalized eruption like one that had occurred two years previously which had lasted several months. At the onset of the disorder it had involved the wrists only. There had been recurrences at various times until a year previously, when it had appeared on the left shoulder and spread to the face. There had been itching for the past six months. The skin of the whole body was dry and infiltrated, with the exception of the palms and soles. The eruption consisted of a large number of polygonal, flat-topped, closely set papules. There was almost total loss of hair on all parts of the body. There was a group of pinhead sized whitish, flat papules on the roof of the mouth. There had been improvement in the subjective symptoms, and the eruption had become less in extent and lighter in color following injections of mercuric chlorid.

DISCUSSION

DR. MOOK said he thought this was a difficult case to diagnose. A great many colored people came to their clinic, and a case of diffuse generalized papular eruption of this kind was occasionally seen. The primary lesion was a slate colored, elevated papular infiltration, more like hypertrophic lichen than any other condition, but he had never seen this condition of the scalp. Cases had been reported in which it had been found on the face and forehead, but he had never seen or heard of a case so extensive as this one. Dr. Mook said he would not like to make a diagnosis without further study. To him, clinically, it looked more like hypertrophic lichen than any other condition.

DR. ZEISLER said he thought it might be mycosis fungoides.

DR. MCEWEN said it was very hard to diagnose these cases in negroes, but he agreed with Dr. Zeisler that it might possibly be mycosis fungoides.

PARAPSORIASIS (PLAQUE TYPE). Presented by DRS. ORMSBY and MITCHELL.

A man, aged 32, had had lesions on the sides of the trunk for the past four months. There was no subjective sensation. There had been no treatment. The patient was in perfect health so far as could be determined.

The eruption consisted of symmetrical, pale, yellowish red, slightly scaling, fairly well defined, oval patches, averaging in size from 5 to 10 cm. in the long

axis. There were a few lesions on the inner surfaces of the upper arms. The back was free from lesions. There were also lesions on the anterior surfaces of the thighs extending to the knees.

DISCUSSION

DR. MCEWEN was inclined to think of parapsoriasis as the diagnosis. He thought the duration, four months, rather long for pityriasis rosea.

DR. SENEAR said he thought it was a case of parapsoriasis.

A CASE FOR DIAGNOSIS. Presented by DR. ZEISLER.

A woman, aged 52 years, who had been operated on a year previously for exophthalmic goiter, had an eruption that had been present on the arms for about fourteen months. There was a congested looking area on the forearm and numerous small translucent whitish papules on the extensor surfaces of the arms.

DISCUSSION

DR. MCEWEN said this case called to mind one he had seen at the Rush clinic a year before. A woman with exophthalmic goiter of eight years' standing had had two operations, without relief. Seven months before her appearance at the clinic she had been operated on a third time, following which the typical symptoms disappeared. Four months later a keratosis of the palms and soles began; this condition was well marked at the time of her seeking advice. The case was clearly one of hypothyroidism following removal of too much thyroid tissue. In this case of Dr. Zeisler's the symptoms showed that hyperthyroidism was still present following the operation for its relief. In fact, it was quite possible that the operation had nothing to do with the eruption.

DR. ZEISLER said that a biopsy had revealed some round cell involvement but no cystic change. He was unable to make a diagnosis.

LYMPHANGIOMA CIRCUMSCRIPTUM. Presented by DRS. ORMSBY and MITCHELL.

A girl, aged 11, had had lesions on the left shoulder since birth. There was no sensation. She had been treated by various methods before coming under observation, without improvement. Over the left shoulder was a band of reddish yellow, superficial, elevated lesions which when punctured emitted a serous fluid. The lesions varied in size from that of a pinhead to that of a match head. These were grouped in areas about 2 cm. in diameter. There were two dime-size verrucous and keratotic masses in two of the groups.

DERMATITIS HERPETIFORMIS. Presented by DR. STILLIANS.

A girl, aged 8, had an eruption on the arms, back and legs which had been present since June. Groups of vesicles or small bullae had been present on the outer side of the left upper arm, the outer side of the right leg, the upper part of the back and over the clavicles. A fresh group was then in front of the right ankle, rather deep bullae, not leaving ulcers and not infiltrated. On the leg and left arm the patches were infiltrated, deep red and crusted. On the back and chest, at the site of former lesions, were thin atrophic scars, so thin as to resemble patches of leukoderma. On the outer sides of the thighs were a number of scaly macules about 15 cm. in diameter, slightly reddish yellow.

DISCUSSION

DR. STILLIANS said that he presented the case as a dermatitis herpetiformis which had been scratched. The child scratched and dug out the lesions so that they left a scar in some instances. He would keep the case under observation.

LUPUS ERYTHEMATOSUS WITH AN EXTENSIVE ERUPTION ON THE TRUNK. Presented by DRS. ORMSBY and MITCHELL.

A boy, aged 12, first seen in March, 1923, at that time had fairly characteristic lesions of lupus erythematosus on the nose, cheeks and ears. Tincture of iodin had been applied prior to observation, after which new lesions had developed in the areas irritated. He was next seen on September 1 and gave a history of having been severely sunburned about July 1. Since then the eruption had changed little in appearance.

At the time of presentation the face was diffusely pigmented and reddened, somewhat edematous over the cheeks and eyelids. The hair of the scalp was sparse and brittle. Over the trunk in the region not covered by a very low-cut swimming suit were numerous slightly elevated pigmented macules in which the follicles were definitely keratotic.

DISCUSSION

DR. LIEBERTHAL said he thought the lesions on the nose and ears were strikingly suggestive of lupus erythematosus. He did not wish to express an opinion as to the manifestations on the rest of the skin.

DR. MOOK said he agreed with the diagnosis.

DR. ORMSBY said the symptoms exhibited by this patient resembled those present in a patient who had been shown before the society about ten years previously. This patient had had lupus erythematosus disseminatus involving the face, hands, forearms, arms and, to a moderate degree, the upper portion of the trunk. Much pigmentation followed the earlier lesions. The case presented today differed chiefly in lack of involvement of the extremities. Dr. Ormsby said he thought that disseminated lupus erythematosus in a child of this age was unusual, but the condition resembled that disorder. They had expected to show today another patient, a child, aged 6, with lupus erythematosus of the discoid type. It might be that this disease occurred more often in children than had formerly been recognized.

BURNING TONGUE. Presented by DRS. ORMSBY and MITCHELL.

A woman, aged 65, had first been seen in August, 1922, with typical leukoplakia of the dorsal surfaces on the left side of the tongue. She had been treated with radium in September, 1922. The leukoplakia entirely cleared up. At the time of presentation she complained of a severe burning in the margins of the tongue. A complete physical examination revealed no abnormalities either locally or in general.

DISCUSSION

DR. MOOK said that some years ago Dr. Engman had separated out a class of troublesome cases and diagnosed them as burning tongue, in which there were no lesions. As a rule, the patients were neurotics, and most of them had no lesions. In some cases there was a mild dermatitis. In these cases they had seldom been able to do anything to relieve the sensation or to cure the disease. The patients seemed to get an idea that they had cancer, and when they became convinced of that, it was up to the physician to do his best to disillusion them.

Dr. Ormsby said that after their attention had been called by Dr. Engman to these cases they had been seeing them occasionally. The treatment had usually been unsatisfactory. Some had recovered after tonsillectomy.

LEPROSY. Presented by Dr. Stillian.

A Chinaman, aged 36 years, who had been shown to the society about six months previously, was shown again because of a recent itching eruption on the backs of his hands and on the arms and body. He had received intramuscular injections of ethyl esters, with slight improvement.

On the backs of the hands and the extensor surfaces of the forearms were thickly set, but discrete, flat, round papules about 0.3 cm. in diameter, a dull brownish red. They were less thickly distributed over the shoulders.

BERLIN DERMATOLOGICAL SOCIETY

Session of Jan. 9, 1923

Dr. Buschke, *in the Chair*

BROMODERMA TUBEROSUM VEGETANS. Presented by Dr. Bruhns.

A young patient with epilepsy who had taken bromids for several months developed typical lesions on the face and along the extensor surfaces. A pyodermite végétante (pemphigus vegetans) was first considered until the surface turned distinctly papillary.

MULTIPLE PRIMARY SPINDLE CELL SARCOMAS. Dr. Heller.

A patient who had had a tumor surgically removed from his left foot three years ago, developed about twenty pea-sized smooth skin tumors. Histologically there was seen a new formation of vessels which were partly cavernous. There was also an accumulation of pigment. In the discussion, Dr. Buschke was reminded of leukosarcomatosis, and he believed the present case was an angiosarcoma.

Session of Feb. 13, 1923

ANAPHYLACTIC ERUPTION FOLLOWING INTRAVENOUS CALOMEL MEDICATION. Presented by Dr. Rosenthal.

Following intravenous injections of colloidal calomel, a generalized urticaria and ecchymoses were provoked along the lower extremities.

TREATMENT OF PSORIASIS WITH INTRAVENOUS SODIUM SALICYLATE INJECTIONS. Dr. Rosenthal.

Twenty per cent. injections of sodium salicylate are particularly effective in removing psoriasis scales, thereby enabling the application of weak chrysarobin ointments (0.25 to 0.5 per cent.). In the discussion, daily injections of a 2 per cent. sodium salicylate solution was advised, as the higher concentrated solution in several instances caused painful thrombosis of the veins.

March 13, 1923

DR. FISCHER, *in the Chair*

IDIOPATHIC SKIN ATROPHY. DR. FISCHER.

A woman, aged 56, developed a painful erythematous swelling on the arm. After the swelling had died down the skin became white and atrophic. Six months later a painful swelling of the left elbow, left knee, and left ankle took place. Later, in the same sequence, the corresponding joints of the right side were involved. There was hyperesthesia in the erythematous areas and hyperesthesia in the atrophic parts, which led to the assumption that these disturbances originate in the central nervous system and are in some way connected with the sympathetic nerve. In the discussion, Dr. Pulvermacher held that idiopathic skin atrophy or acrodermatitis chronica atrophicans and scleroderma are due to endocrin disturbances. Dr. Arndt called attention to the observation in 95 per cent. of the cases the patients are women. Dr. Buschke said he believed that an involvement of the sympathetic nerve is probable, as this disturbance is frequently found combined with scleroderma in which sympathectomy has proved so successful therapeutically.

EXTENSIVE DIFFUSE LEUKODERMA PSORIATICUM. DR. LANGER.

This disorder cannot be differentiated clinically from leukoderma syphiliticum, especially as during the last few years leukoderma has frequently been observed with the generalized form of psoriasis.

GRANULOMA ANNULARE. DR. ARNDT.

There was a positive Pirquet reaction which pointed to the possible tuberculid nature of this disorder. Dr. Arndt advised surgical excision as the best measure.

SOFT CHANCRE ON THE RIGHT INDEX FINGER. DR. HEYN.

The disorder clinically resembled sporotrichosis and tuberculosis. Streptobacilli were found. Attention was called to the fact that region buboes are rare in extragenital soft chancres.

Session of May 8, 1923

DR. ARNDT, *in the Chair*

ICHTHYOSIFORM CONGENITAL ERYTHRODERMA. DR. ARNDT.

A man, aged 23, had suffered since his birth from hyperkeratosis of the palms, extensor surfaces of the fingers, elbow and knees. Cornified orifices of the coil glands were visible. The condition was related to keratoma palmare et plantare. Clinically, it is difficult to differentiate from pityriasis rubra pilaris and from psoriasis in some cases. The long duration and the fact that the disturbance begins with birth are of diagnostic value.

DEMONSTRATION OF A SECTION THROUGH A TOPHUS. Dr. Arndt.

The patient developed a dry scaling eczema and alterations typical of gout. With each attack of gout the eczema flared up.

TWO CASES OF PSORIASIS PROBABLY DUE TO ENDOCRIN DISTURBANCES. Dr. Buschke.

In Case 1 there were rupioid, partly pustular, psoriasis lesions. Medication with thyroid extract and mild local treatment effected a cure. Case 2 was one of typical psoriasis and excessive adipositas. Medication with hypophysis extract caused a loss of 20 pounds (9.07 kg.) of weight and cleared up the skin.

ESSENTIAL ANGIECTASIS AFTER GUNSHOT WOUND. Dr. Buschke.

A shot in the head had probably destroyed the central vasomotor centers, which probably caused the telangiectatic spots on the left arm and left thigh of the patient.

COLOGNE DERMATOLOGICAL SOCIETY

Session of Jan. 26, 1923

Dr. Fischer, *in the Chair*

EPIDERMOLYSIS BULLOSA HEREDITARIA. Presented by Dr. Fischer.

The patient was treated systematically with the carbon arc light, which caused pigmentation and complete cure. Most of the discussors preferred the carbon-arc lamp. Dr. Dreyer called attention to Arning's method. Arning injected soluble bismuth preparations and effecting a cure in two cases.

LUPUS ERYTHEMATODES. Dr. Fischer.

This case, which had withstood all therapeutic measures for years, was treated with neo-silverarsphenamin. The inflammatory symptoms quickly disappeared, while the old lesions remained uninfluenced. In the discussion, Dr. Meirowsky advised treatment of the remaining pigmentations with radium, which leaves white cicatrices at the site of the pigmentations.

LUPUS HYPERTROPHICUS OF THE FACE. Dr. Zinnser.

This was a demonstration of a case in which tuberculin injections combined with roentgen-ray irradiation furnished satisfactory results.

SYPHILIS RESISTANT TO ARSPHENAMIN. Dr. Zinnser.

This case proved that spirochetes can become arsphenamin resistant. In these cases, decoctum Zittmannii is advised, also bismuth, as well as a change in the arsphenamin preparation.

ALBUMINURIA FOLLOWING CHRYSAROBIN TREATMENT. Dr. Zinnser.

The use of chrysarobin ointments in the case of a child was immediately followed by albuminuria.

GERMAN DERMATOLOGICAL SOCIETY IN THE CZECHO-SLOVAK REPUBLIC

Session of Feb. 4, 1923

DR. KREIBICH, *in the Chair*

DEMONSTRATION OF THE LOCAL EFFECT OF A SUBCUTANEOUS INJECTION OF A NEO-ARSPHENAMIN PROCAIN SOLUTION. DR. SOBOTKA.

The neo-arsphenamin was dissolved according to the method advised by Cabannes and Chavannez in ten times the quantity of a 1 per cent. solution of procain. It was then injected into the thigh. A painful reaction with reddening and swelling occurred, the pains lasting for six days after the injection.

SKIN CARCINOMAS IN A SCAR DUE TO BURNS. DR. SCHOENHOF.

Dr. Schoenhof presented a case in which an extensive carcinoma had developed on a scar caused by a burn. He reported three other similar cases.

CYLINDROMA OF THE CHEEK. DR. SCHOENHOF.

A woman, aged 60, had for the last ten years suffered from hemispherical tumors under the skin of the cheek. Histologically these were basalcell carcinomas which resembled the cylindromas of the scalp described by Spiegler, Frieboes and Watanabe. These tumors are congenital.

Session of March 4, 1923

DR. KREIBICH, *in the Chair*

NONTUBERCULOUS FORM OF ERYTHEMA INDURATUM. Presented by DR. WAELSCH.

A patient, aged 63, without any symptoms of tuberculosis, developed a dark red hard infiltration on one of the lower extremities. The blood picture was normal. There were no varices or symptoms of a phlebitic process.

NEURODERMITIS. DR. WAELSCH.

A woman had suffered for twenty years from a lichen simplex chronicus on the arm. Four years ago, intensely itching, brownish red nodules developed on the arm, which left small follicular scars.

TUMOR-LIKE LUPUS ERYTHEMATODES HYPERTROPHICUS. DR. WINTERNITZ.

Four years ago the first lesions developed, involving the face, ear and scalp. Palpation revealed deep seated tumor-like thickening of an histologic lupus erythematodes.

PAPILLOMATOSIS CUTIS. Dr. Zuleger.

A patient, aged 23, had a defect of the right half of the prepuce. Beginning at the frenulum, there was a dollar sized, tumor-like proliferation of hard consistency and papillary structure. Histologic investigation showed acanthosis, parakeratosis, proliferation of the connective tissue and infiltration with round cells.

Session of April 15, 1923

POSITIVE SPIROCHETE FINDINGS IN AN INTRA-URETHRAL INFILTRATION. Dr. Winternitz.

Secretion taken from the pars pendula penis contained typical *Spirochetae pallidae.*

SCLERODERMA EN PLAQUES WITH ACROCYANOSIS. Dr. Waelsch.

A woman, aged 38, suffered from acrocyanosis and paresthesia of the extremities ("dead finger"). She also developed sclerodermatous thickening of the skin on the fingers and arms. There were numerous angiectases in the face. As the thyroid gland was underdeveloped and the menses irregular, organotherapy will be tried.

REFRACTORY SYPHILIS PRAECOX. Dr. Pick.

In spite of energetic combined antisyphilitic treatment, a patient developed a gumma nasi which is still progressing in spite of arsphenamin and mercury medication. The patient is cachectic, runs high temperatures and has recently developed multiple periostitic lesions on the tibia and ulna.

ARSPHENAMIN DERMATITIS. Dr. Schoenhof.

A patient developed, after the fifth injection of neo-arsphenamin, although the kidney function was normal, a slightly itching pityriasis rosea-like eruption. After the eighth injection, a sudden general dermatitis developed.

CICATRICES FOLLOWING THE USE OF GENERALIZED VACCINE. Dr. Schoenhof.

A girl, aged 8, developed numerous variola scars on the forehead and left cheek. At the age of 1, it was fed by its mother who was vaccinated at this time. The child was not vaccinated on account of an impetigo contagiosa. In the site of the impetigo lesions, vaccine pustules developed which caused the scar formation.

Session of June 10, 1923

Dr. C. Kreibich, *in the Chair*

CUTIS MARMORATA. Dr. Kreibich.

Dr. Kreibich presented a case of pronounced marbled cyanosis on the extensor surfaces of the arms, legs and cheeks. In a warm room the symptoms disappeared. The function of the heart was normal.

LUPUS PSEUDOPERNIO. Dr. Kreibich.

Dr. Kreibich presented a case of lupus vulgaris of the cheek and lupus tumidus of the nose, with cyanosis and dilatation of the vessels. Tuberculin caused a reaction in the lesions.

CICATRICES FOLLOWING FAVUS. Dr. Schoenhof.

A patient developed numerous irregular deep atrophic cicatrices on the scalp among which numerous small exostoses were palpable. The cause was ascribed to a favus.

PSORIASIS VULGARIS TREATED WITH SODIUM SALICYLATE. Dr. Zuleger.

Intravenous injections of sodium salicylate sensitize the skin and increase the effect of weak chrysarobin ointments. Ointments of 0.25 per cent. prove sufficiently effective when injections are given. The veins are occasionally irritated in spite of a good technic and dilution of the salicylate compound.

VIENNA DERMATOLOGICAL SOCIETY

Session of Feb. 8, 1923

Dr. Fasal, *in the Chair*

LATENT SYPHILIS (POSITIVE WASSERMANN) IN COMBINATION WITH ERYTHEMA INDURATUM BAZIN. Presented by Dr. Sachs.

A syphilitic patient developed chestnut sized erythema induratum nodes on both lower extremities. Specific antisyphilitic treatment reduced the erythema lesions to half their size after one "course." The case is interesting because: (1) The positive Wassermann reaction could easily induce one to consider the nodes as syphilitic gummas. (2) It shows the remarkable influence of a therapy which is not specific for tuberculosis.

CHEIROPOMPHOLYX WITH A CONSIDERABLE INCREASE IN BLOOD SUGAR. Presented by Dr. Krueger.

The skin on the palms and soles was reddened, dry and covered with numerous pinhead sized vesicles filled with a yellowish fluid. Some of the eruptions resembled erythema multiforme. The blood sugar showed a distinct increase.

LIVEDO RACEMOSA. Dr. Urbach.

The patient, who had never had any medicinal treatment, developed also a black, hairy condition on the tongue. In the discussion, Dr. Oppenheim said that he had produced experimentally a black hairy condition of the tongue by administration of tincture of rhatany. This tincture contains rhatany red as well as rhatany tannic acid, which cause the cornification and blackening of the papillae filliformes. The rhatany ointment used for epithelization of large surface wounds is based on this principle. Potassium iodid, which cures black hairy tongue, has the property of dissolving corneous substances.

MALIGN, MELANOTIC, NEVOGENOUS TUMOUR OF THE BUCCAL MUCOSA WITH METASTASES IN THE LYMPH GLANDS OF THE NECK. Dr. Arzt.

Black discolorations in the buccal mucosa rapidly developed into large tumors with metastases in the lymph glands. Histologic examination revealed numerous pigment cells in the connective tissue as well as nevus cells.

Session of March 1, 1923

Dr. Balban, *in the Chair*

NETLIKE LIVEDO. Dr. Rusch.

A woman who had contracted syphilis seven years before and who had had several recurrences, although the serum reaction was negative, developed a pigment on the inner surfaces of both lower extremities corresponding to a cutis marmorata. These were preceded by scaling nodular infiltrations, part of which were still present. The affection belongs in the group of netlike livedos for which numerous etiologic factors are assumed. In the foregoing case the spirochetes were assumed as the causative factor although specific treatment did not influence the clinical picture. In the discussion, Dr. Spitzer said that he had seen pictures similar to cutis marmorata develop after pellagra. The netlike pigmentation develops also on surfaces that are never exposed to sunlight.

LICHEN VIDAL. Dr. Rusch.

A systematized lichen Vidal responded rapidly to neo-arsphenamin medication.

APLASIA CUTIS CONGENITA WITH PERIPHERAL SPOTTED PIGMENTATION. Dr. Oppenheim.

A girl showed a dollar sized bald white patch on the forehead the periphery of which was surrounded by ephelis-like spots. The picture corresponded to the one described by Dittrich, Voerner and Riehl, only the peripheral pigmentation seems to be unusual.

MILIARY GUMMA OF THE MUCOSA. Dr. Kren.

The buccal mucosa showed numerous small flat nodular infiltrations, the surface being slightly ulcerated and resembling tuberculosis. The Wassermann reaction was positive. Topical and general mercury medication caused rapid improvement.

LICHEN RUBER PLANUS HEALED WITH FEVER. Dr. Kren.

Dr. Kren treated three cases exclusively with milk protein injections, and obtained better results than with arsenic. Six injections were given within three weeks.

Session of March 15, 1923

DR. ARZT, *in the Chair*

NEVUS (ICHTHYOSIFORMIS) OF THE ENTIRE BODY. DR. KRUEGER.

A patient developed widespread zoster-like nevi from the shoulder down to the sacral region. The lesions resembled ichthyosis.

CONNECTIVE TISSUE NEVUS. DR. RUSCH.

A palm-sized nevus showed histologically an hypertrophy of the collagenous tissue and the sebaceous glands.

SCIRRHOUS MAMMAE WITH SKIN METASTASES. DR. RUSCH.

A scirrhus of the right mamma was surrounded by skin metastases. In the discussion it was stated that metastases corresponding to the lymph vessels in the area immediately surrounding tumors are rare. The clinical picture in this case resembled herpes zoster on account of cystic alterations.

LIVEDO LENTICULARIS. DR. RUSCH.

In this case the influence of radiant heat was assumed as the probable etiologic factor. Histologically, there were no particular alterations, except a pronounced acanthosis and hyperkeratosis. In the discussion Dr. Kerl assumed a general damage of the skin vessels; he believed the pigmentation was due to a thermal influence similar to the disturbances seen after application of thermophores.

LYMPHOGRANULOMATOSIS WITH NONSPECIFIC ITCHING SKIN ALTERATIONS. DR. ARZT.

The patient, who ran high temperatures for weeks, had tuberculosis of the lungs and pronounced adenitis, particularly in the regions of the neck and groin. The skin was pigmented and itched severely. Excision of a gland revealed collagenous alterations and the histologic picture of lymphogranulomatosis.

Session of May 3, 1923

DR. FASAL, *in the Chair*

ERYTHEMA MIGRANS. DR. BALBAN.

A small nodule on the abdomen of the patient developed within ten days into a palm-sized, oval, bluish red lesion. The surface was smooth and without infiltration. In the center a small nodule was visible. In 1911, Balban described several cases in which the same disturbance had been caused by insect bites. A similar cause was assumed in this case.

PRESSURE ATROPHY OF THE SKIN OF THE NECK CAUSED BY A COLLAR BUTTON; STRIATE DISTENSAE. DR. OPPENHEIM.

A dollar sized unpigmented cigaret paper-like skin was caused by pressure in the region of the collar button. There were also numerous striate distensae ad nates and around both knee-caps. The elasticity of the skin tissue in general had been affected.

GRANULOSIS RUBRA NASI AND FUNCTIONAL HYPERHIDROSIS OF THE NOSE. Dr. Urbach.

This case seems to support the opinion of Darier that granulosis rubra nasi is a consequence of hyperhidrosis.

ISOLATED PSORIASIS VULGARIS OF THE PALMS AND SOLES. Dr. Porias.

Irradiation of the thymus (one tenth followed by one fifth of an erythema dose) caused improvement, but the condition recurred.

A CASE OF DISSEMINATED LICHEN RUBER PLANUS CURED WITH INJECTIONS OF NONSPECIFIC MILK ALBUMIN. Dr. Nobl.

The first two intramuscular injections caused a flaring up of the lesions. Three weeks later a third injection effected distinct regression.

Session of June 7, 1923

Dr. Balban, *in the Chair*

ALLERGY OF THE SKIN TO SILK. Dr. Perutz.

Contact with any kind of silk, whether dyed or not, caused an itching papulo-urticarial dermatitis. In the discussion, Dr. Oppenheim said that silk contains a substance of unknown composition which causes toxicodermas in workman employed in silk factories. Dr. Perutz explains this dermatitis as an allergy of the skin against a silk protein (serizin) an albuminous substance contained in silk.

LEPRA MIXTA. Dr. Bruenauer.

The case was interesting because the exact incubation period could be determined. A girl from Jaffa had come into contact with lepers six years before and had developed the first disturbances four years later. She had tuberous lepromas on the chin and fingers, macular dark red brownish infiltrations, chiefly on the upper and lower extremities. The Wassermann reaction was positive, while the blood picture showed a pronounced increase in lymphocytes. Dr. Bruenauer, in the discussion, reported another case in which a woman, who had lived for years with her husband who suffered from lepra tuberosa, had borne several healthy children and was not in the least affected by the leprosy.

LICHEN SPINULOSUS AND ALOPECIA. Dr. Porias.

A laborer in a rubber factory developed a lichen spinulosus on the neck, arms and trunk. This was followed by a sudden almost complete alopecia of the scalp, arms and hands. The cause of the disturbance was ascribed to the influence of benzin vapors, which damaged the hair follicles. In the discussion, Dr. Oppenheim reported similar cases of benzin damage.

PSORIASIS VULGARIS OSTRACEA. Dr. Oppenheim.

The skin of a girl, aged 15, showed circular figures covered with huge masses of yellow, turbid, corheous substances, with deep fissures resembling a crocodile skin. The elbow and knees showed typical scales. Lang termed this form of psoriasis "ostracea," Kaposi "scutularis" and Anderson "rupioides."

MULTIPLE TUMOR-LIKE CORNIFIED PAPILLOMAS OF THE LEG FOLLOWING GUNSHOT WOUND. Dr. Oppenheim.

After receiving a gunshot wound in the ankle the patient developed along the achilles tendon a chain of small red dry nodules firmly adherent to the skin. Histologic examination pointed to papillomas. Hyperkeratosis, acanthosis, papillary proliferation, new formation of connective tissue and slightly inflammatory symptoms were present.

Book Reviews

DISEASES OF THE GUMS AND ORAL MUCOUS MEMBRANE. By Sir Kenneth Goadby, K.B.E., M.R.C.S., L.R.C.P., Lecturer on Bacteriology of the Mouth, Dental Department, University College Hospital. Cloth. Price, $14. Pp. 383, with illustrations. New York: Oxford University Press, 1923.

This is an unusually comprehensive treatise on mouth diseases, well illustrated by eight plates in color and 106 in black and white. It is a compilation, largely from the author's own writings, together with extensive borrowed material from almost all fields of medical and dental science. The title gives only a slight idea of the scope of the work. Much space is given to syphilis, infection with *Actinomyces*, neuralgias, alveolar abscesses, sprue, tumors, pyorrhea alveolaris, roentgenography, vaccines, histology and bacteriology. Without detracting in the least from the worth of the book, it may be said that there is little in it that is new, its principal value being due to the fact that the author has presented in convenient form most of the diseases of the mouth, both primary and secondary; also the causative relation of oral infection to disease elsewhere in the body. While the author has generously quoted Black, Rosenow, D. J. Davis, Talbot and a few other noted American authors, he has not discriminated so wisely in the choice of some others to whom he has given greater preference. Billings' writings on secondary infections are not mentioned. Noyes' work on histology also is not mentioned and this omission seems strange, since Noyes demonstrated the chain of lymphatics in the peridental membrane. The author strangely speaks of Vincent's angina of the gums. Vincent's angina is not a disease of the gums. Angina is from angio, a prefix indicating a relation with a vessel, usually a blood vessel. Vincent's angina, in medical and other dictionaries, is defined as "a disease of the throat similar to diphtheria but occasioned by a different microbe." Although much space is given to "trench mouth" (Vincent's angina, used synonymously), no mention is made of the fact that in an article published in the *Dental Review* (Chicago), 1906, this disease was first described and there named "acute ulcerous gingivitis." Later, Tunnicliff demonstrated that the fusiform bacillus and spirillum was the organism that causes the disease. The author condemns hydrogen peroxid in the treatment of "trench mouth." Since the organism causing this disease is an anaerobe, it seems that the free oxygen liberated by the application of hydrogen peroxid would make it the medicament of choice, and its value, in this connection, has been positively demonstrated. On page 18 the author says, "Films made from the interdental spaces . . . show no signs of pus cells." This statement will confuse the American reader who thinks of films as dental roentgenograms. What the writer means is smears for microscopic examination. Favorable mention is made of the use of vaccines in the treatment of primary oral infections and secondary diseases in other parts due to these infections. Their use for such conditions was generally abandoned in America some years ago, since they proved to be unsatisfactory. Neoplasms of the mouth are treated in the conventional manner; early recognition and surgical removal are very properly recommended. The more modern treatment of pyorrhea alveolaris, or, as the author prefers to name this disease, "periodontitis," is not included;

that is, the elimination of the pockets by cutting back the gums to the bottom of the pockets. The book is recommended to those who do not possess an extensive library and to those who need a ready reference work to oral diseases.

Review from J. A. M. A., Dec. 8, 1923.

DISEASES OF THE SKIN. By FRANK CROZIER KNOWLES. Second Edition. Price, $6.50. Pp. 595 with 229 illustrations, 14 plates. Philadelphia: Lea & Febiger, 1922.

The appearance of a second edition is evidence of the deserved popularity of this book. It is an excellent shorter treatise of the diseases of the skin. The work is a conservative statement on the subject of dermatology by an experienced dermatologist. It is embellished by a large number of illustrations from photographs of unusual excellence. Altogether the work is to be commended.

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